Frederic S. Lee.

QUAIN'S

ELEMENTS OF ANATOMY

EDITED BY

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IN THREE VOLUMES.

VOL. I.—PART II.

GENERAL ANATOMY OR HISTOLOGY

BY PROFESSOR SCHÄFER.

ILLUSTRATED BY NEARLY 500 ENGRAVINGS, MANY OF WHICH ARE COLOURED

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GENERAL ANATOMY, OR HISTOLOGY.

GENERAL ANATOMY, OR HISTOLOGY.

By E. A. SCHÄFER.

General Anatomy, or as it is now more commonly termed Histology, is that branch of Anatomy which treats of the structure of the textures. As has already been explained in the Introduction to this volume, the body of every one of the higher animals is made up of organs adapted for the performance of its several functions, and these organs are themselves composed of various tissues or textures. In order that the structure of any organ or part of the body should be understood, it is necessary to study, both together and separately, the several tissues of which it is composed, so as to ascertain their composition and the manner in which they are combined to constitute the organ or part in question. This is chiefly effected by minute dissociations and thin sections, which are observed with the aid of the microscope, and hence the terms "Minute Anatomy" and "Microscopic Anatomy" are also applied to this branch of the science. It is found that when the body is thus dissected and analyzed by the aid of the microscope, that the number of distinct tissues which are met with is comparatively small, and some of these again, although at first sight to all appearance distinct, yet have so much in common in their structure and origin one with another (forms of transition also being met with between them), that the number becomes still further reduced. The elementary tissues which may be thus enumerated are as follows :—

The epithelial tissues.
The connective tissues.
The muscular tissues.
The nervous tissues.

Particles which are met with in the fluids of the body, such as the corpuscles in the blood and lymph, are also described amongst the elementary tissues.

Many of the organs are formed wholly of a single one of these elementary tissues, or with a comparatively slight intermixture of others. Thus the muscles are made up almost entirely of muscular tissue, with but a small intermixture of connective tissue, blood-vessels and nerves; whilst the cartilages are composed wholly of a variety of connective tissue. On the other hand, there are certain organs or parts of the body not in themselves distinguished by the preponderance of any special tissue, but compounded of two or more in varying proportion, the structure of which it is nevertheless convenient to describe along with the tissues, on account of their wide distribution in the body, and their uniformity of structure in different parts. Such are :—

Blood-vessels.
Lymphatic vessels.
Lymphatic glands and bodies of like structure.
Serous membranes.
Synovial membranes.
Secreting glands.
Mucous membranes.
Integument.

Every texture taken as a whole was viewed by Bichat (Anatomie générale, 1801) as constituting a peculiar system, presenting throughout its whole extent in the body characters either the same, or modified only so far as its local connections and uses render necessary ; he accordingly used the term "organic systems" to designate the textures taken in this point of view. Of the organic systems above enumerated some are found in nearly every organ ; such is the case with the connective tissue, which serves as a binding material to hold together the other tissues which go to form an organ ; the vessels, which convey fluids for the nutrition of the other textures, and the nerves, which establish a mutual dependence among different organs. These were named by Bichat the "general systems," to distinguish them from others such as the cartilaginous and osseous, which being confined to a limited number or to a particular class of organs, he named "particular systems."

Structural elements.—When any tissue is separated by the aid of the microscope into the simplest parts which possess assignable form, such parts are termed the structural elements of the tissue. In almost every tissue, some at least of these structural elements retain to a certain extent the characters of the elementary corpuscles of which the whole body is originally composed. These structural elements are named the "cells" of the tissue. Others again lose for the most part those characters, and becoming elongated and modified in structure are termed the fibres of the tissue, whilst in other cases, fibres are formed not from the cells but between them. Except the epithelium, all the tissues have fibres as characteristic structural elements, and some, as the connective tissue, fibres of more than one kind. But structurally and chemically as well as functionally, the fibres of the several tissues differ widely from one another.

Intercellular substance.—In addition to these separable structural elements, many of the tissues are composed of a homogeneous matrix or ground substance, in which the structural elements are imbedded. This matrix may exist in considerable quantity, as in some varieties of connective tissue, or on the other hand it may be almost imperceptible in amount, serving merely as a cementing material to connect together the individual tissue-elements, as in epithelium. From its softness, clearness and homogeneity, this ground substance is often apt to escape observation, but its existence may always be rendered evident in consequence of the property it exhibits of combining with salts of silver, a brown deposit of metallic silver occurring in it on subsequent exposure to the light (v. Recklinghausen).

Since all the animal tissues however diversified they may appear, originate as collections of the elementary corpuscles or cells above spoken of, and since these cells remain, many of them, as constituent elements of the formed tissue, we must first of all consider minutely what it is that constitutes an animal cell, what is its structure, its chemical composition, its physical and vital properties, and how it becomes reproduced and multiplied.

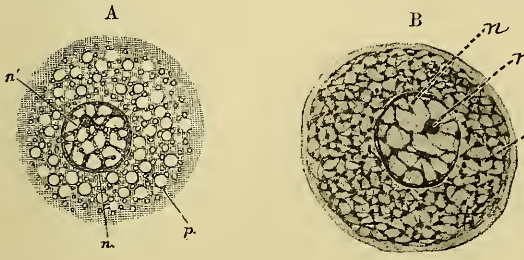
THE ANIMAL CELL.

An animal cell is a corpuscle of microscopic dimensions, the cells of the human body seldom exceeding $\frac{1}{300}$th of an inch in diameter, and many being as small as one-tenth of this or even less. But whether small or large, every cell consists of two distinct parts : of the main substance of the cell, which has received the name of *protoplasm* (fig. 201, *p*), and of a minute vesicular structure, generally placed near the centre of the cell, and termed its *nucleus* (*n*).

THE PROTOPLASM OF THE CELL.

Structure of the cell-protoplasm.—Until comparatively recent years it was universally held that the principal or living substance of the cell to which the name

of *protoplasm* is applied is a completely homogeneous material, which, although it might contain granules of solid matter or globules of watery fluid (vacuoles) imbedded in it, is nevertheless itself entirely devoid of structure (fig. 201, A). It is possible that this view may still hold good for some cells both animal and vegetable, but in most cells, especially those which are "fixed" or non-amœboid, it is found that a differentiation of the protoplasm has occurred in such a manner that a part of it appears under high powers of the microscope in the form of a network or spongework,



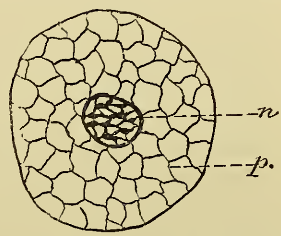


Fig. 201.—A, Diagram of a cell, the protoplasm of which appears structureless, but is occupied by vacuoles and granules. B, Diagram of a cell, the protoplasm of which is composed of spongioplasm and hyaloplasm.

p, protoplasm ; *n*, nucleus ; *n'*, nucleolus.

Fig. 202.—Cell from the epidermis of an embryo of salamandra, treated with 1 per cent. hydrochloric acid. (After Kölliker.)

n, nucleus, with network of chromoplasm ; *p*, protoplasm, showing a reticulum of plastin.

whilst the rest of the protoplasm occupies the meshes of this network (figs. 201, B, and 202). The network is known as the *reticulum* or *spongioplasm;* while the substance which occupies its meshes may be designated the *enchylema* (Carnoy) or *hyaloplasm.*

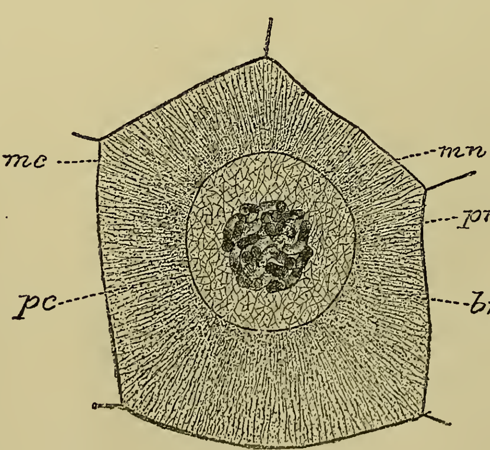


Fig. 203.—Cell with radially disposed reticulum from the intestinal epithelium of a worm. (Carnoy.)

mc, membrane of the cell ; *pc*, protoplasm of the cell ; *mn*, membrane of the nucleus ; *pn*, achromatic substance of the nucleus, with the convoluted chromatin filament, *bn*, contracted into the centre.

The proportion which these bear to one another varies in different cells, but it may be stated that as a general rule the amount of spongioplasm becomes augmented as the development of the cell proceeds, and that the younger a cell the greater is the relative amount of hyaloplasm.

The shape and size of the meshes of the reticulum also vary in different cells, and even in different parts of the protoplasm of the same cell. Thus in some cells the constituent fibrils or cords of the spongioplasm are disposed radially from the nucleus to the periphery (fig. 203), and the meshes are radially elongated ; in others they are disposed evenly in all directions, whilst in some a concentric disposition of the fibrils can be determined. The fibrils are invariably united together (as is implied by the use of the term reticulum) into a network, and at the nodes of the network where

they join one another they may be slightly enlarged. These enlargements at the junctions of the fibrils as well as the optical sections of those fibrils which are coursing in a direction more or less parallel to the visual axis of the observer appear, when the horizontally running fibrils are not clearly seen, as distinct points or granules in the protoplasm ; it is perhaps for this reason that the cell-substance was formerly constantly described as being finely granular.

The external layer of the protoplasm of many cells, especially that of fixed cells like those which constitute the varieties of epithelium, and in a notable degree the cells of the higher plants, may become altered by the deposition in or upon it of chemical substances which render it firmer and more resistant than the rest of the cell. In this way a cell-membrane (fig. 203, *mc*) may be formed, either complete or, more commonly, furnished with minute pores which allow of the passage of fluid or the connection of the cell with its neighbours by filaments of protoplasm which traverse the pores. In those cases where a cell-membrane is formed the peripheral layer of the protoplasm is usually furnished with a denser reticulum than the rest, but this is not the case in cells like the white corpuscles of the blood and the amœba which have no cell-membrane. In these the exterior of the protoplasm may be clearer than the interior, indeed a reticulated appearance may be altogether wanting in it, or may be replaced by a few radial striæ. Such clearer peripheral protoplasm is sometimes known as the "ectoplasm" to distinguish it from the granular-looking "endoplasm" around the nucleus.

Chemical nature of protoplasm.—Protoplasm may contain imbedded in its substance (generally in the hyaloplasm) various adventitious materials, such as granules of proteid or starch, globules of fat, crystals of various kinds, pigment-granules and globules of watery fluid (vacuoles). These may have been formed by the cell either from its own substance or directly from materials imbibed in a fluid form, or they may have been bodily incepted in the solid form, but they are not essential to its composition, although no doubt when they occur they play an important part in relation to its vital activities.[1] Apart from these the protoplasm of all vegetable and animal cells, since it is similar in its functional manifestations, is also in all probability similar in chemical constitution. So far as the proteids are concerned, it would appear that there is a preponderance of the less stable members of that group, such as globulins and albumoses as distinguished from the more stable albumins, and that these cell-proteids appear to be associated with ferment-like reactions like those which produce digestive or coagulative changes. The chief proteid found is a muco-globulin, containing phosphorus, to which the name *plastin* has been applied. It would further seem that the presence of certain inorganic substances, and especially calcium, is essential to the life and therefore to the functions of protoplasm, but in what manner the lime may be combined with the organic basis of the living material, remains as yet quite undetermined. It must further not be forgotten that water enters very largely into the composition of all living material.[2]

CHEMICAL AND PHYSICAL CHANGES. AMŒBOID MOVEMENTS.

Vital phenomena of protoplasm.—During the life of a cell its protoplasm is constantly undergoing chemical and physical changes. The chemical changes are in some measure determinable by comparing the products which are given off by the

[1] The terms "deutoplasm" and "paraplasm" (Kupffer) have sometimes been applied to materials contained within a cell, which are not considered to constitute a part of the actual protoplasm.

[2] For an account of the present state of knowledge regarding the chemistry of protoplasm and of the cell generally, consult Halliburton, "A Textbook of Chemical Physiology," 1891, pp. 190 to 211.

cells of a tissue with the nutritive material which they absorb. In all the higher animals this nutritive material is the blood or lymph, but the products which are formed are not entirely the same for all cells, since they vary in some measure with the specific activity of the cell ; thus the cells of the salivary glands yield the saliva, those of the mammary gland milk, and those of the liver form, besides other substances, glycogen. But all protoplasm, whatever may be its specific function, has this in common, viz., that it absorbs and combines with oxygen, and yields carbon dioxide and other products of oxidation, and as a result of these processes of oxidation heat and other kinds of energy are produced. These chemical changes are always more marked as the functional activity of the cell becomes increased, and accordingly any circumstances which tend to promote the activity of protoplasm, such as warmth, electrical or other stimulation, the action of certain drugs, tend proportionally to increase the activity of its chemical processes. One general chemical property of living protoplasm is that by virtue of which it is able to assimilate and eventually to convert into its own substance non-living proteid material. In this manner the protoplasm of a cell may increase in amount, or in other words the cell may grow ; but if the amount of protoplasm does not permanently increase, this is due to the fact that just as much protoplasm is being broken down and removed from the cell as is added by the process of assimilation. Chemical processes which involve the building up of living material within a cell have received the general name of *anabolic* changes ; those on the other hand which involve the breaking down of such material into other and simpler products are known as *katabolic*. By the *metabolism* of a cell is understood the sum of all the ana- and katabolic changes which are proceeding at any time within it.

Amœboid movements.—The most obvious physical changes seen in living protoplasm are those which are designated "amœboid." This term was derived from the freshwater amœba, the protoplasm or sarcode of which has long been known to exhibit spontaneous changes of form, accompanied by a flowing or streaming of its soft semifluid substance. The phenomenon was in fact described by Rosenhof in 1755, but the similar movements of the cell-protoplasm of the higher animals was only recognised much later (in 1846 by Wharton Jones, who noticed the amœboid movements of the white blood-corpuscles of fish). If the protoplasm of the cell is enclosed by a membrane its movements are necessarily confined within the limits of such cell-wall, and the actual changes which are in these cases observable consist in a streaming or flowing of the soft living substance, such flowing being rendered obvious by the carrying along by the stream of any minute particles which may be imbedded in the protoplasm. The term "rotation" has been given to a movement of this kind which is observed in many plant-cells, and is of a very regular character, and usually in a determinate direction ; but in animal cells the intrinsic streaming movements are less regular and usually less obvious in character. It is, however, on the other hand in those animal cells which are unprovided with a cell-wall (free or naked cells) that what may be termed the amœboid movements proper present themselves, and in none more strikingly than in the pale blood- or lymph-corpuscles. If one of these be observed under a high power of the microscope it will be seen gradually to protrude a portion of its protoplasm at one part or another, and sometimes at several places simultaneously. These protrusions (*pseudo-podia*) may be presently withdrawn again and others given out, or a pseudopodium which has been protruded at any one part of the corpuscle may extend itself further, and the main part or body of the corpuscle may pass gradually towards and into the extending pseudopodium. By a repetition of this process the cell may glide slowly, away from its original situation, and move bodily along the field of the microscope so that an actual locomotion thereby results. In this manner the white corpuscles may, even while the blood is circulating, pass through the walls of the capillaries and

minute veins and find their way into the surrounding connective tissue, where they may further continue to exhibit amœboid movements. Corpuscles which have thus emigrated from the vessels are known as "wandering cells," and the process of emigration is known as "diapedesis." Although probably occurring to a certain extent normally, it is greatly increased in inflammatory conditions of the tissues.

Inception of foreign particles.—When any foreign particle comes in contact with a free cell, the particle adheres to it, becomes enwrapped by processes of the protoplasm, and is then drawn gradually into the interior, where it may remain for some time without change, being moved about by any currents which exist in the cell, and carried along by the changes of place which the cell undergoes (see fig. 204). Eventually such foreign particles may be extruded again. If, on the other hand, the particle is of considerable size as compared with the protoplasm with which it comes in contact, the latter extends around and over it so as to envelop it more or less completely. This phenomenon of inception seems thus to be dependent upon amœboid movements of the protoplasm.

Conditions influencing the contractile manifestations of protoplasm.—All the several manifestations of contractility are influenced in the same manner by

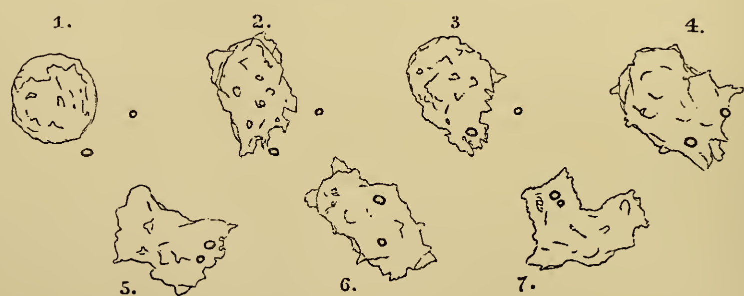


Fig. 204.—Changes of form of a white corpuscle of newt's blood, sketched at intervals of a few minutes. The figures show also the intussusception of two small granules, and the changes of position which these underwent within the corpuscle. (E.A.S.)

similar external conditions. Thus it is found that variations of temperature have a marked effect upon all. In warm-blooded animals the phenomena cease altogether to be exhibited, if the protoplasm which is under observation is cooled to below a temperature of about 10° C., although they will be resumed on warming the preparation again, and this even if it has been cooled to 0° C., or a little lower. And when warmed gradually, it is found that the movements become more active as the temperature rises, attaining a maximum of activity a few degrees above the natural temperature of the body, although if maintained at an abnormally high temperature, they are not long continued. A temperature a little above this maximum, rapidly kills protoplasm, producing a stiffness or coagulation in it (heat-rigor) which is preceded by a general contraction. From the condition of rigor the protoplasm cannot be recovered.

The contractility of protoplasm is dependent upon supply of oxygen. If this be withheld, the movements will, it is true, proceed for a time as usual, but this is because protoplasm, like other forms of contractile substance, such as muscle, has the power of storing away and using oxygen in some form of combination. For it is found that the active manifestations will not proceed indefinitely in the absence of oxygen, but cease after a time, to be renewed only on the accession of fresh oxygen.

Many reagents in solution influence the activity of protoplasm. Some of these act by adding to or subtracting from the water which it contains. As a general rule the imbibition of water up to a certain point, varying according to the source of the protoplasm which is under observation (Thoma), accelerates the activity of the protoplasm, but beyond that point addition of water produces a destructive effect. A comparatively slight amount of desiccation is, so far at least as regards the protoplasm of the higher animals, destructive of vitality, but this statement does not hold good for the protoplasm of many of the lower animal and plant organisms.

Amongst reagents acids, although very weak (even carbonic acid), stop the contractile manifestations; alkalies, on the other hand, if sufficiently dilute, increase at first their activity. They are stopped by chloroform and ether, but may be again resumed on the removal of those vapours. Some poisons (*e.g.*, veratria) rapidly arrest the movements of cells.

Effect of electrical and other stimuli upon protoplasm.—The effect of electrical stimulation upon protoplasm which is exhibiting either amœboid or streaming movement is, if sufficiently strong, to cause an immediate cessation of those movements, accompanied by a withdrawal into the main substance of any processes that may have been protruded. If the stimulation cease the movements will recommence, provided the shock has not been so severe as to injure the living substance.

Abrupt changes of temperature, and mechanical stimulation, such as is produced by sudden pressure or harsh contact, act in a similar manner.

Further considerations regarding the structure of protoplasm.—If the pseudopodia of a white blood-corpuscle are observed with a high power of the micro-

Fig. 205.—An amœboid pale corpuscle of the newt, killed by instantaneous application of steam, showing the structureless appearance of the pseudopodia. (Drawn by D. Gunn.)

scope, they appear when first thrown out from the body of the corpuscle to be perfectly clear and homogeneous as if composed of hyaloplasm alone. Subsequently the reticular part of the protoplasm may flow into the pseudopodium. This structureless character of the pseudopodia can be well observed if a preparation of the blood of the newt be made and set aside for half-an-hour or more until the white blood corpuscles have had time to throw out broad flattened pseudopodia which spread themselves over the under-surface of the cover-glass. If now a jet of steam be allowed to play for a moment upon the cover-glass, these corpuscles are instantly killed without having been able to withdraw the pseudopodia. They can then be hardened and stained, and observed with the highest powers of the microscope, when it is found that the thin extended portions of protoplasm show no trace of structure but appear completely homogeneous, in decided contrast with the main part of the cell, which exhibits distinctly the spongio-plasmic network.

Stricker has lately published a photograph of the white blood-corpuscle of a Proteus anguineus, which demonstrates the same fact. In this photograph, which was taken from the living amœboid cell by an instantaneous method, the body of the cell, which is nearly spherical, is beautifully reticular, whilst a thin external layer and a pseudopodium, which is being protruded, appear completely homogeneous.

From this it is clear that the pseudopodial protoplasm, that namely to which the more obvious activity of the cell is immediately due, is structureless, and, probably, composed of hyaloplasm alone. The amœboid movements are produced by a flowing of this hyaloplasm, which may extend, as in many Rhizopods, far beyond the limits of the spongioplasm. But if the corpuscle is subjected to artificial stimulation of any kind (electrical, mechanical. thermal) the pseudopodia are withdrawn into the body of the corpuscle, which then becomes spherical and appears wholly reticular. The spherical form of the corpuscle represents, therefore, the completely contracted condition ; it is only in the absence of any obvious source of excitation that the cell throws out pseudopodia. Since the spherical condition is produced by mechanical stimuli, it is probable that the impacts which the white blood-corpuscles are constantly receiving in the circulating blood maintain them in the spherical form which they always exhibit within the vessels, and immediately the blood is drawn. It may also be that the inception of foreign particles by amœboid cells is produced by the excitation which their contact produces upon the portion of hyaloplasm to which they adhere, causing its contraction and withdrawal into the spongioplasm.

To sum up :—The protoplasm of an amœboid cell is composed of two substances—spongioplasm and hyaloplasm. The spongioplasm has a reticular appearance and sponge-like structure, an affinity for staining fluids, is firmer and more refractile than the hyaloplasm, and is probably highly extensile and elastic, but not actively contractile.[1] The hyaloplasm, on the other hand, appears structureless, has little or no affinity for stains, and is highly labile and fluent. It is the active flowing movements of the hyaloplasm which produce the well-known phenomena of amœboid activity. The spongioplasm forms a sort of framework which serves to support the hyaloplasm, and into which, under the influence of stimuli, the hyaloplasm may become entirely withdrawn. In non-amœboid cells the hyaloplasm does not extend beyond the limits of the spongioplasm. The latter is the "œcoid," hyaloplasm the "zooid," to adopt terms which Bruecke has introduced into histology, although with a somewhat different signification (see p. 242).

The question has been frequently discussed whether we are to regard the spherical condition as that of rest, and the amœboid condition as that of activity, or *vice versâ*. Viewed by the light of the above statements it is clear that both are manifestations of activity, both being produced by flowing of hyaloplasm. In the one case this flows into the pores of the spongioplasm ; this is the condition which corresponds to the contraction of muscle ; in the other case the hyaloplasm flows out of the spongioplasm, producing a condition corresponding to the extension of muscle after contraction.[2]

Whether one or other of the two substances is ever wholly absent from the protoplasm of cells is a question which cannot at present be decided. There are cells and unicellular organisms, both animal and vegetable, in which no reticular structure can be made out, and these *may* be formed of hyaloplasm alone. In that case, this must be looked upon as the essential part of protoplasm. So far as amœboid phenomena are concerned, it is certainly so ; but whether the chemical changes which occur in many cells are effected by this or by spongioplasm is another matter.

The movements within plant cells must also be regarded as due to the flowing of hyaloplasm. It is, indeed, impossible to conceive that the contraction of a reticulum could produce the circulation of the protoplasm which is seen within a cell of *Vallisneria*. How the flowing is produced is an entirely different question, and one which must at present remain unanswered.

Quincke has shown that if a drop of solution of albumin surrounded by an envelope of oil is placed in water a soapy film forms at the junction of the oil and water, and the drop

[1] Carnoy and many other histologists have assumed that the spongioplasm or reticulum is the contractile part of protoplasm, and that the hyaloplasm is passive. If this were the case electrical excitation should cause the reticulum to shrink and to squeeze the hyaloplasm out of its meshes whereas the contrary is the case, the hyaloplasm passes into the meshes of the spongioplasm, which become thereby enlarged.

[2] In dealing with the structure of muscle it will be shown that here also as in protoplasm there is a passage of a substance resembling hyaloplasm into and out of a porous spongioplasm. It will further be presently shown that the activity of cilia, can also be explained by assuming a flowing of the cell-hyaloplasm into and out of the cilia, so that all these forms of contractile phenomena can be brought into the same category.

exhibits changes of form due to alterations of surface tension, which are comparable to the amœboid movements of living cells. Still more recently, Bütschli has found that if oil is rubbed up into a paste with certain alkaline salts in a moist condition, and some of the paste is examined in water, the latter diffuses into the paste and converts it into a froth, which, under the microscope, has an appearance not unlike the reticular part of protoplasm. In such a froth streaming movements may be seen, lasting for a considerable time, and changes of form may occur in the mass, due partly to continued diffusion through the soap-like envelopes of the froth-bubbles or vacuoles, and partly to the bursting of these bubbles when they become enlarged and approach the edge of the mass. Upon these observations Bütschli has based a theory that all protoplasm has such a vacuolated froth-like structure, that the reticulum is only apparent, being the optical expression of the material between the vacuoles, and that the movements of protoplasm are produced by physical and chemical processes analogous to those which cause the movements within the froth of oil and salt-solution which he has employed. Whilst admitting the interest of Bütschli's observations, it would, I think, be unwise to follow too far the deduction which he is inclined to draw from them. For amongst other important objections which might be urged, the absence of reticular appearance, and, therefore, of frothy structure from the active protoplasm of pseudopodia is in itself fatal to the theory. This difficulty Bütschli meets by assuming that such structure is really there although the thinning out of the pseudopodia has rendered it invisible. But the line of junction of the spongioplasm and hyaloplasm of an amœboid cell is sharp (fig. 205), and shows no tendency to fade off gradually into the pseudopodia, as on Bütschli's assumption it should unquestionably do.

Nägeli, on theoretical grounds, has conceived that the essential living substance must in its ultimate (ultra-microscopical) structure consist of solid particles (or systems of such particles) surrounded by material of fluid consistence. To these hypothetical particles of living matter (or to the systems which they form) he has given the name *micellæ* (*tagmata*, Pfeiffer), and he supposes that they may, like the substances known as ferments, produce chemical changes in materials which are in contact with them without themselves undergoing any permanent or perceptible change (catalytic action).

THE NUCLEUS OF THE CELL.

The nucleus is a minute vesicular body, placed generally near the centre of the cell and embedded therefore in the protoplasm. In form it is round or oval in most cases, but it may be elongated and folded or irregular in shape. Its size relatively to that of the cell varies much in different instances, for sometimes there is so small an amount of protoplasm that the nucleus appears to occupy nearly the whole cell. This is the case with many of the cells which are met with in lymphatic glands, and with the small nerve-cells which are found in the cerebellum and elsewhere. On the other hand, the protoplasm of the cell, whether altered as in the superficial layers of some stratified epithelia, or unaltered as in many of the white corpuscles of the blood, may much exceed the nucleus in bulk. In absolute size, the nucleus does not exhibit so considerable a variation as do the cells of the same animal. There are, however, some notable exceptions ; thus the nucleus is absolutely much larger in the ova and in many nerve-cells than it is in other cells of the body.

Structure of the nucleus.—In the typical "resting" condition the nucleus is always bounded by a well-defined wall, which encloses the nuclear contents. These are of two kinds, formed and amorphous. To the latter the term *nuclear fluid* is sometimes applied, and the former may be conveniently termed *chromoplasm* (nucleoplasm or karyoplasm of authors) ; this term is used to include also the substance which forms the wall of the nucleus. But it is by no means certain that the homogeneous amorphous substance which occupies the interstices of the chromoplasm is entirely fluid, so that it is better termed *nuclear matrix.* It is very possible that this homogeneous matrix of the nucleus may be of the same nature as the hyaloplasm of the cell-substance if indeed it is not actually continuous with it, but the chromoplasm is not the same as the spongioplasm of the cell-substance.

The chromoplasm usually takes the form of a network of fibres connected externally with the nuclear wall. One or more strongly refracting granules or globules, which are named *nucleoli*, may be suspended, isolated, in the nuclear matrix, or they may be connected with one another, if they are more than one, and with the nuclear wall by the network of fine filaments just spoken of (fig. 206). Some authors regard the nucleoli as mere local accumulations of the chromoplasm,

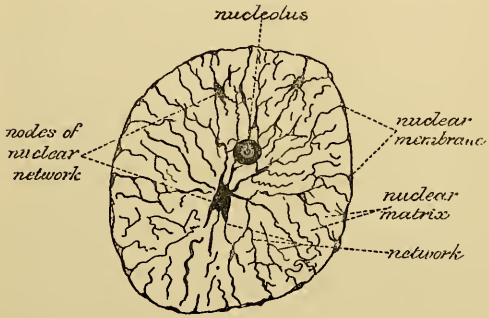


Fig. 206.—Diagram of resting nucleus. (Waldeyer.)

Fig. 207.—Cell-nuclei, exhibiting the reticulate appearance of the karyoplasm. (Flemming.) *a*, nucleus of liver-cell (carp) ; *b*, nucleus of a connective tissue cell.

differing only in size from those which occur at the nodes of the network. Others, relying upon certain differences in their behaviour to staining fluids, look upon the nucleoli as altogether distinct in nature and chemical composition.

Spontaneous changes of form may occur in nuclei. Thus both Flemming and Stricker have described, in preparations of blood, nuclei, which had been set free by rupture of the corpuscles to which they belonged, exhibiting spontaneous changes of form, and Klein has made a similar observation upon the large nuclei of the glands in the skin of the triton. Within the living epithelium-cells of the tail of salamander-larvæ, Flemming also noticed alterations taking place in the outline of the nuclei. Several observers have remarked spontaneous changes of form in nucleoli, which they have compared to the amœboid movements of protoplasm.

Although most so-called "resting" nuclei, *i.e.*, nuclei which are not at the time in process of division by karyokinesis, exhibit the well-marked reticular appearance just mentioned, some are occasionally met with in which the nuclear filaments are

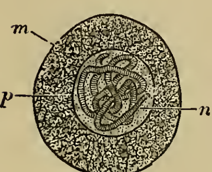


Fig. 208.—Gland-cell from a larva of Nemocera. (Carnoy.) *m*, cell-membrane ; *p*, protoplasm ; *n*, nucleus with convoluted filament.

not united with one another to form a network, but have the appearance of a convoluted skein (fig. 208), which may either consist of a tortuous filament or of several distinct looped and contorted threads. When thus formed of a number of looped filaments it may frequently be noticed that one side or pole of the nucleus is left clear of the filaments, the loops of which are set around this pole (fig. 209, A), while their free ends interdigitate at the opposite pole (antipole, fig. 209, B). It is thought probable by Rabl, who has pointed out these differences at the two poles of the nucleus, that this condition is really the typical one, and that it occurs in most nuclei, but that the primary loops of chromoplasm send out secondary twigs in all

directions, which interlace and join with one another throughout the nucleus to form the reticulum which is usually observed (fig. 209, c). When, however, a nucleus is about to undergo division by karyokinesis these secondary twigs become again with-

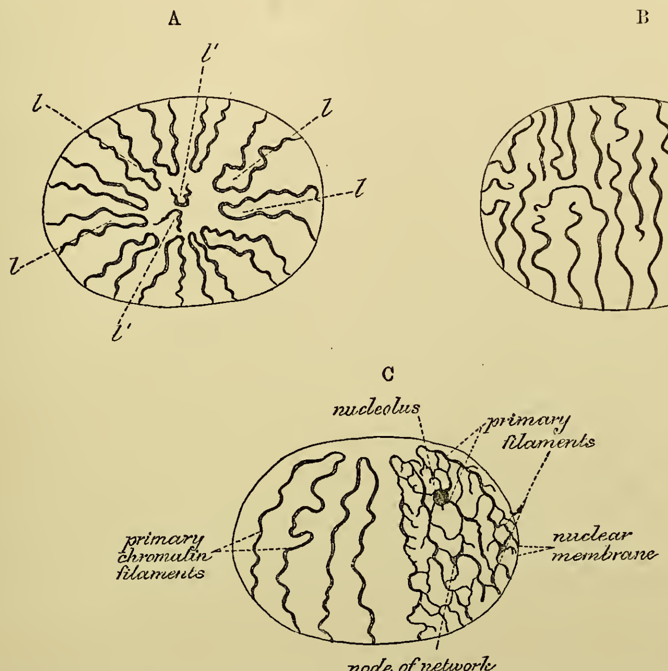


Fig. 209.—Diagrams to show the general arrangement of the chief chromatic filaments in a nucleus. (Rabl.)

A, nucleus viewed at the "pole" end; l, l, looped extremities of the chromatic filaments; l', l', irregular filaments.

B, nucleus viewed at the "anti-pole" end. The free ends of the chromatin loops are seen interdigitating.

C, nucleus viewed from the side, the "pole" end being uppermost. On the left side only the primary filaments are shown; on the right side the secondary filaments, which produce the network of the resting nucleus, are represented.

drawn into the parent loops of chromoplasm, and the typical arrangement of the loops becomes manifest.

The nuclear filaments are not structureless, although it is difficult to make out any structure in them when they form a close reticulum. But when they form a convolution or skein within the nucleus they are often sufficiently large and evident to permit a definite structure to be made out. Indications of such structure were first described by Balbiani in salivary cells of an insect-larva (Chironomus), in which the convoluted nuclear filaments show well-marked transverse striations as if made up of alternate dark and light bands. When this appearance is more closely investigated it is found to be due to the existence of minute, highly-refracting particles, which are imbedded in regular series in a clear homogeneous matrix (fig. 210). These particles have a strong affinity for colouring matters, and it is in virtue of their presence that the nuclear filaments become deeply stained by hæmatoxylin, safranin, and other substances; hence the material of which they are composed is known as *chromatin*, or chromatic substance, and the remainder of the nucleus is termed in contradistinction *achromatin*, or achromatic

substance. The chromatin is sometimes in the form of fine particles, which are arranged in a linear manner to form filaments.

The term chromatin was originally employed by Flemming to denote the whole substance of the chromoplasmic filaments, but since it has been shown (by Carnoy and others) that those filaments are actually composed of two substances, one stainable and the other remaining unstained by most dyes, it is advisable to restrict the use of the term in the manner above indicated. The particulate structure of nuclear filaments was first noticed by Pfitzner in the V-shaped loops of certain dividing nuclei.

As to the membrane bounding the nucleus, this has been regarded by most authors as a distinct wall shutting it off from the protoplasm of the cell. Others look

Fig. 210.—Part of the nuclear filament of the cell shown in fig. 208. Greatly magnified. (Carnoy.)

upon it as being merely a dense superficial portion of the chromoplasmic network, and therefore as not complete, but rather of the nature of a basket-work permitting of intercommunication between the cell-hyaloplasm and the nuclear matrix. Others, who admit the incompleteness of this chromoplasmic membrane, yet describe a complete enclosing membrane of achromatic substance separating the nucleus from the cell-protoplasm.

Chemical nature of the nucleus.—Not much is known regarding the chemical nature of the cell nucleus. Miescher described in the nuclei of pus cells a substance to which he gave the name *nuclein*, which is characterised by the resistance which it offers to most chemical reagents, especially to acids and digestive juices, and by its containing a considerable quantity of phosphorus. This substance is in all probability identical with Flemming's chromatin. The achromatic material of the chromoplasmic fibres, which has received the name of *linin*, has been conjectured to be similar to the plastin which is found in cell-protoplasm. The composition of the nuclear matrix and of the spindle of achromatic fibrils which makes its appearance in the nucleus during karyokinesis is completely unknown, but the fibres of the spindle are probably composed of linin.

The nucleus has been supposed by some histologists to be identical in nature with protoplasm. Its behaviour, however, with many reagents is altogether different; and in general it may be said that it offers greater resistance to their action than the substance which surrounds it. Moreover, its chromoplasm stains much more intensely with hæmatoxylin and many other reagents, than does protoplasm, and, on the other hand, it remains in some cases unstained by reagents which colour protoplasm intensely, for example, solution of chloride of gold. So that chemically at least there is a considerable difference between the nucleus and the protoplasm. But if we regard the spontaneous changes which are manifested by both, and especially the important part which the nucleus plays in the division of the cell, as will be immediately described, there is much in favour of the view which regards the nucleus as a portion of the living substance somewhat altered in chemical nature, which is set aside to preside over the reproduction of the cell, and perhaps also over other functions. In favour of this view there are observations which show that under certain circumstances, the nucleus may enlarge at the expense of the protoplasm, even to the extent of absorbing the greater part of the latter, so that the whole cell is little else than nucleus; indeed, this relative increase of size of the nucleus seems to be a change which constantly precedes the phenomena of cell-division.

Functions of the nucleus.—Various observers have described in the cells of secreting glands and elsewhere, a spherical body which is either partly attached to the nucleus or is at least closely connected with it. This has been spoken of as the *paranucleus* (German, *Nebenkern*), and it is described as having been

derived from the nucleus of the cell, although the exact manner of its formation is not clear. Important functions in connection with the nutrition and functions of the cell generally have been ascribed to the paranuclei, but further investigations are needed in order to show how far their occurrence is general, and what is the precise nature of the part they play in the economy of the cell.

The general question whether the nucleus of a cell has any functions beyond those concerned with the reproduction and division of the cell also requires further elucidation. The existence of animal cells or organisms without nuclei has been affirmed by various authors, but in all but the lowest animals and plants every cell is undoubtedly nucleated. Attempts have been made with more or less success to separate off portions of cell-protoplasm without nuclei, and to keep them for some time under observation with the microscope. It is stated that under favourable circumstances the separated protoplasm will continue for a while to live, and will exhibit amœboid movements, but that it does not grow nor form a cell-membrane (vegetable cells), although the part of the cell which still contains the nucleus enlarges to the original size of the whole cell, and does form a new cell-membrane. In the case of the amœba it has been found that the portion deprived of a nucleus will take in food-particles as before, but does not digest them (Hofer), nor are its amœboid changes so pronounced as in the part which still has the nucleus. The action of the contractile vacuoles continues, however, unaltered. From this it has been inferred that the presence of the nucleus is necessary to the growth and nutrition of protoplasm, and that it may therefore be concerned to a certain extent in regulating the anabolic processes of the cell as well as its division and reproduction. In the ovum of Dytiscus, Korschelt has observed an intimate relationship between the formation of food-granules within the ovum and the protrusion of pseudopodium-like processes from the nucleus, and infers from these observations that the nucleus may be directly concerned in the assimilation of nutriment. But whatever other functions it may possess there is no doubt that the most obvious function of the nucleus is connected with the division and multiplication of the cell.

THE DIVISION AND MULTIPLICATION OF CELLS AND NUCLEI.

Direct and indirect division of nuclei.—According to the scheme of cell-division which was formulated by Remak, the division of the cell is preceded by the division of the nucleus, which forms by a simple process of constriction two equal parts, and this again is initiated by the previous division of the nucleolus. The essence of this scheme consists in the simple fission of the nucleus, which directly divides to form two smaller or daughter nuclei : it is commonly spoken of as the process of " direct " division.

The term " indirect " division has been given on the other hand to a process which is of very wide and almost universal occurrence in both animal and plant cells, in which the chromoplasm undergoes previously to the fission of the nucleus a series of remarkable changes, the ultimate result of which is the separation of its chromatin into two exactly similar portions, which go respectively to form the chromatin of the daughter nuclei. Concomitantly with these changes in the nucleus the protoplasm of the cell also exhibits active changes, which ultimately result in its accumulation around each of the daughter-nuclei and the formation of two separate cells. To the changes which are undergone by the nucleus in this " indirect " process of division the name *karyokinesis* was given by Schleicher : the appearances which the nuclei present at different stages of karyokinesis are spoken of as *mitoses* [1] (Flemming).

[1] μίτος, a thread. The indirect process of division is also termed " mitotic," and the direct is known in contradistinction as " amitotic."

With the discovery of the wide-spread occurrence of karyokinesis there was for a time a tendency manifested to deny altogether the possibility of the more direct and simple process of nuclear fission. It is now usually held that this simpler process may occur, although it is not easy to adduce entirely satisfactory evidence of amitotic instances of nuclear division. No doubt elongated nuclei are frequently to be seen with two nucleoli and with a constriction, more or less pronounced, in the middle, partially dividing them into two parts, but hitherto no competent observer has seen and described all the stages of simple fission proceeding in one and the same nucleus in

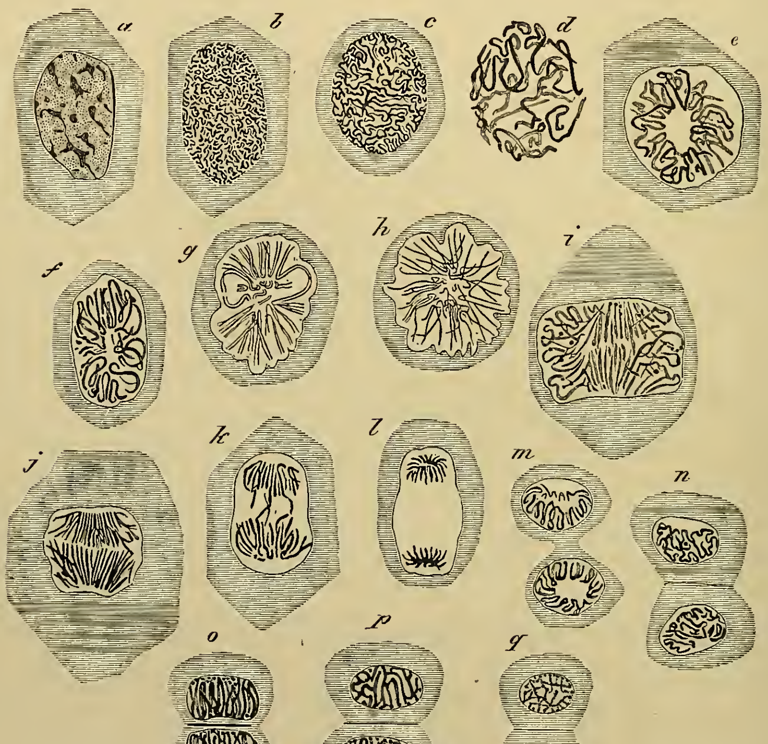


Fig. 211.—Epithelium-cells of salamander-larva in different stages of karyokinesis. The cells were hardened in picric or chromic acid, and stained with hæmatoxylin or safranin. Highly magnified. (Flemming.)

a, resting cell, showing the nuclear network; *b*, first stage of division, the chromoplasm transformed into a skein of closely contorted filaments; *c*, second stage, filaments larger and less closely arranged: in this and all the other figures except *a* the nuclear matrix is clear; *d* (rather more magnified than the rest), filaments larger and showing an arrangement in loops: this is more evident in *e*, where they collectively have a rosette-like appearance enclosing a central clear space; *f*, filaments converging towards the centre; *g*, stellate phase or aster; *h*, completion of longitudinal splitting of the filaments which is already beginning in *f* and *g*; *i*, commencing separation of filaments into two groups (metakinesis); *j*, further separation into two sets; *k*, separation more advanced; *l*, stellate phase of daughter-nuclei (dyaster); *m*, commencing convolution of the filaments; *n*, filaments more contorted; *o*, *p*, gradual passage of daughter-nuclei into condition of rest (network, *q*). The division of the protoplasm is seen to begin in the stage represented by *m* and to be rapidly completed (at *n*).

the manner in which the process was believed to occur prior to the discovery of the mitotic process. Lymph-cells were for a time often instanced as exhibiting the amitotic changes, but, as it would appear from Flemming's researches, on entirely

insufficient grounds, and most other examples which have been adduced have also failed when subjected to a rigorous investigation.[1]

While, therefore, we are not in a position to deny the occasional occurrence of amitotic nuclear division, it must yet be affirmed that in by far the largest number of cases in all classes of plants and animals cell-division takes place by the mitotic process.

Karyokinesis. Indirect or mitotic division of the nucleus.—The following is a brief account of the more important phases of karyokinesis which have been noticed in typical instances of indirect or mitotic division in animal cells :—

The nucleus of a cell which is about to divide first becomes somewhat enlarged and its chromoplasm loses the net-like arrangement which is usually met with in resting nuclei, and becomes converted into a closely constricted skein of filaments (fig. 211, *b*). There is some difference of opinion as to whether at this "skein" stage there are a number of separated filaments, or whether there is one long filament only. Both the nucleoli and the chromatic nuclear membrane become merged into the skein of chromoplasm, and the outline of the nucleus against the cell-protoplasm becomes in consequence less distinct. According to Rabl, the conversion of the network into the skein is effected by the withdrawal of all the secondary anastomosing chromoplasmic filaments into the primary convoluted loops (fig. 209, C) : the latter therefore become thicker and more evident, and this process of thickening accompanied by shortening of the convolutions proceeds until a far less complex and more open skein is the result

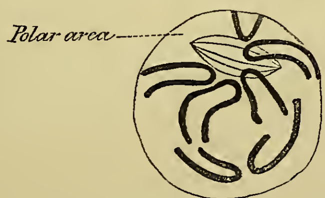


Fig. 212.—Appearance of achromatic spindle in polar area of dividing nucleus. (Rabl.)

Fig. 213.—Movement of spindle towards the middle of the nucleus, accompanied by the V-shaped chromosomes, some of which are already split longitudinally.

(fig. 211, *d*), in which the constituent looped filaments can now be seen and their arrangement relative to pole and antipole of the nucleus made out (fig. 209, A and B). At about this stage of the process of karyokinesis, a spindle-shaped system of achromatic fibrils which is known as the achromatic spindle, makes its appearance at the pole of the nucleus, either taking origin altogether within the nucleus, or arising partly or entirely in the adjacent protoplasm and passing into the nucleus at its polar area (figs. 212 and 213). At any rate the poles of the spindle soon reach as far as or even project beyond the limits of the nucleus on either side, and the achromatic fibres which compose it diverge at either pole from a central particle (fig. 214), the pole-corpuscle, and from this corpuscle on the other hand fibrils radiate outwards into the protoplasm of the cell.

As just stated, the achromatic spindle makes its appearance at the polar end of the nucleus, towards which the loops of the chromoplasmic filaments are directed. Here the spindle is placed obliquely across the polar area, and hence it moves gradually towards the middle of the nucleus, where it eventually takes up its position. In this movement it is accompanied by the chromatic filaments (*chromosomes* of

[1] Instances of amitotic division which have been described in recent years by various authors, will be found referred to in Waldeyer's article on Karyokinesis, in the Quarterly Journal of Microscopical Science, vol. xxx., 1889 ; also in an article by Flemming on the Division of Leucocytes, in the Archiv f. mikr. Anatomie, Band xxxvii., 1891.

Waldeyer), and by the time the spindle has reached the middle of the nucleus, these filaments, now shortened and become distinctly V-shaped, are seen to be arranged in a star-like manner radiating from its equator. This star-like disposition is best seen when the nucleus is viewed in the direction of the axis of the spindle ; the stage is known as that of the *aster* or *monaster* (fig. 215). By the time that this stage is

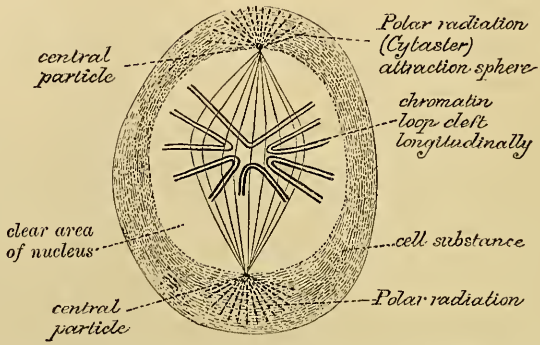


Fig. 214.—DIVIDING NUCLEUS, SHOWING SPINDLE OF ACHROMATIC FIBRES, WITH THE CHROMOSOMES ARRANGED ASTRALLY AT THE EQUATOR OF THE SPINDLE. (Rabl.)

arrived at, and sometimes even while the chromatic filaments still form a convoluted skein, a remarkable change, first noticed by Flemming, is found to have occurred in them, each chromosome having become split along its length into two exactly similar but finer filaments, which remain adherent to one another for a while (fig. 211, *g*, and figs. 213, 214, and 215). There can be little doubt that this cleavage of the chro-

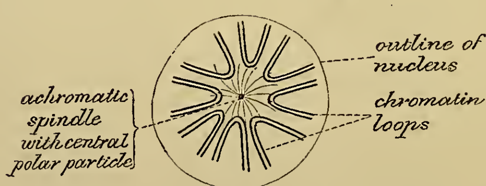


Fig. 215.—DIVIDING NUCLEUS AT "ASTER" STAGE, SEEN FROM ONE OF THE POLES. THE ACHROMATIC SPINDLE IS REPRESENTED FORESHORTENED. (Rabl.)

mosomes is one of the most important of the karyokinetic changes of the nucleus, for the result is that the chromatin is thereby divided into two precisely equal amounts, which pass as the subsequent phases show to the respective daughter-nuclei.

The next stage in the process of karyokinesis has been termed " metakinesis " and consists in the separation of the chromosomes which have resulted from the longitudinal division above described (fig. 211, *i*, *j*, *k*). The separation usually begins at the apices of the V-shaped loops which as they separate become turned towards the poles of the spindle, while the limbs often remain adherent for a time at the equator of the spindle (fig. 216, A and B), and even after separation remain connected across the equator by delicate achromatic uniting filaments (fig. 216, C).[1]

[1] It is now agreed by most observers that these "uniting filaments" are not, as was formerly supposed, parts of the achromatic spindle, but that they are probably spun out from the chromosomes as these pass towards the poles of that spindle. It is assumed that the spindle-fibres shorten, and that this shortening or contraction tends to draw the chromosomes towards each pole. According to v. Beneden and Rabl, the spindle-fibres are very numerous, and Rabl believes them to be attached to the chromatin granules of Pfitzner, of which the chromosomes are made up, the spindle being thus formed of two distinct cones of achromatic fibres.

The chromosomes now pass along the fibres of the achromatic spindle with their apices directed towards the poles of the spindle. The convergent direction which they thus assume as they approach the pole, gives them a star-like appearance when viewed in

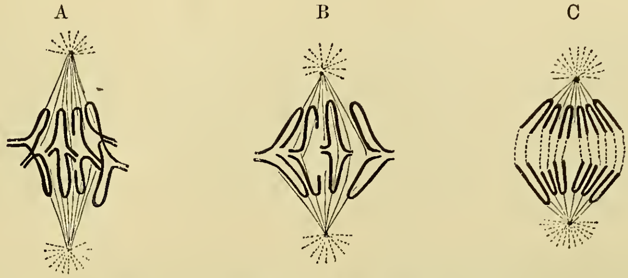


Fig. 216.—Stages of metakinesis. (Rabl.)

A, commencing separation of the split chromosomes.
B, the separation further advanced.
C, the separated chromosomes passing along the fibres of the achromatic spindle.

the axis of the spindle, and since there are now two such converging groups in the original nucleus the stage has been termed the *dyaster* (fig. 211, *l, m*).

In the next phase the chromosomes, which are thus passing to form the daughter-nuclei, tend to become convoluted and to arrange themselves in the manner typical of a resting nucleus, with their loops directed towards one pole (that of the half spindle along which they have passed), and their free ends towards the other pole (fig. 217); if much convoluted they have the appearance of a skein (fig. 211, *n*), but this is not so complicated as that of the mother-nucleus. Finally from the convoluted primary loops of the daughter-nuclei secondary filaments are given off (lower half of fig. 217), which anastomose with one another, and convert the chromoplasm into the network of a resting nucleus (fig. 211, *p, q*).

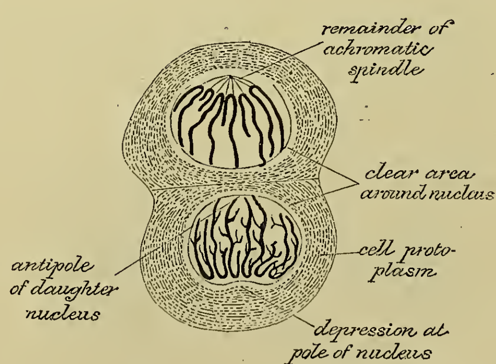


Fig. 217.—Formation of chromatin network in daughter-nuclei. (Rabl.)

In the upper daughter-nucleus the chromosomes are still separate and comparatively simple loops; in the lower one, secondary filaments are growing out from them to form a network. The cell-protoplasm is now completely divided.

The cell-protoplasm divides during or immediately after the stage of metakinesis. Sometimes a constriction is seen around the equator of the cell, and this becomes gradually more pronounced until the division of the cell is complete. In other cases—and this is especially frequent in plant cells, but is also seen in some animal cells (fig. 218, *d*)—points of enlargement make their appearance on the achromatic uniting filaments which connect the daughter-nuclei in the stage of metakinesis, and these points gradually increase in size until they mark a plane of separation between the two halves of the cell, which then divides along this plane.

The above is the typical mode of division by karyokinesis, but there are many varieties. Sometimes, as in most plant cells and in many animal ova, the achromatic spindle is very distinct (fig. 218), and the chromatin is in very small amount, the chromosomes being in the form of short rods instead of relatively long filaments.

The filaments have been described in some instances as splitting transversely instead of longitudinally (Carnoy), but it is uncertain if this is really the case. In the division of the ovum of Ascaris megalocephala (fig. 219), v. Beneden describes the achromatic

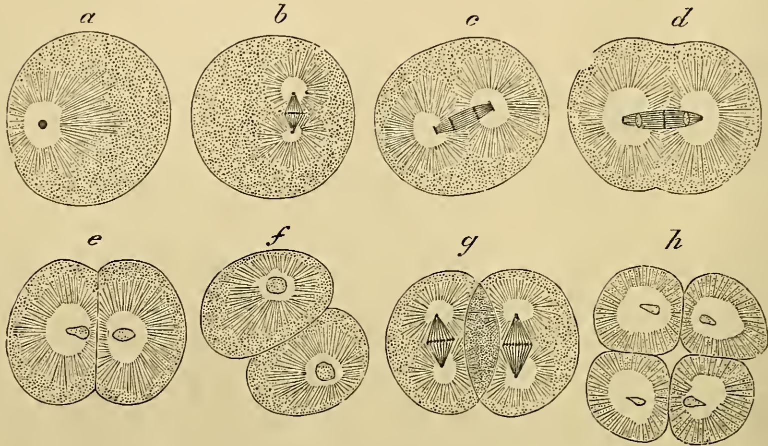


Fig. 218.—Stages in the division of the ovum or egg-cell of a worm. (Strasburger.)

a, ovum before division; *b*, nucleus occupied by a spindle-shaped system of fibres, with chromatin nodules (chromosomes) at the equator of the spindle; *c*, separation of chromosomes into two parts which gradually travel towards the poles of the spindle and there become transformed into new (daughter) nuclei, whilst the protoplasm at the same time also separates into two parts (*d*, *e*, *f*); in *d* thickenings of achromatic fibres in middle of spindle, indicating plane of division of cell; *g*, repetition of the division-process, formation of spindles in daughter-nuclei; *h*, result of the division of these.

spindle as being preceded by the differentiation within the protoplasm of two "attraction-spheres" which surround the pole-corpuscles, but are separated from them by a clear area. When the spindle is developed its fibrils extend from the centre

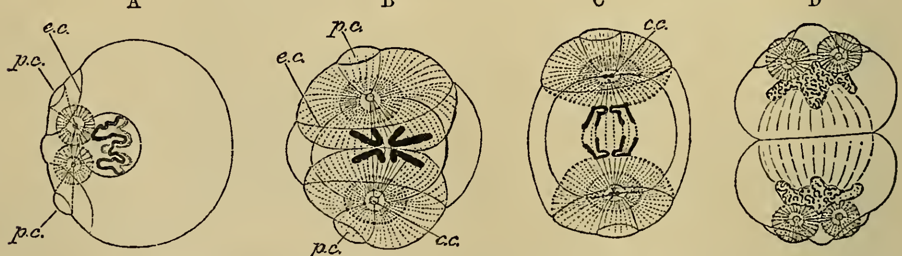


Fig. 219.—Ovum of Ascaris megalocephala in process of division.

A, ovum before division, with the chromosomes of the female pronucleus in the skein condition. Adjacent to the pronucleus are two attraction-spheres, united by an achromatic spindle.

B, the attraction-spheres are now at opposite ends of the ovum: at the equator of the spindle which unites them, four chromosomes are seen. The protoplasm of the ovum, except in the equatorial zone of the cell, is arranged in lines radiating from the centre (central particle) of the attraction spheres.

C, stage of metakinesis. The chromosomes are seen passing along the achromatic spindle towards its poles; the equatorial zone is broader, and the attraction lines extend a less distance in the protoplasm; the central particle of the attraction sphere is divided into two.

D, the daughter-cells are now formed, and the attraction-sphere in each is already divided preparatory to the division of the daughter-nuclei.

e.c., equatorial circle; *p.c.*, polar cone; *c.c.*, pole-corpuscle.

of these attraction-spheres, which thus occupy its poles, towards its equator, and are on the other side prolonged towards the periphery of the protoplasm as a conical

system of fibrils, which v. Beneden terms the polar cone (fig. 219, *p.c.*). Besides these fibres of the spindle and its polar cones, other striæ radiate from the attraction-spheres into the surrounding protoplasm, leaving a somewhat prominent equatorial zone of cell-protoplasm free from radiations, and marked off from the radially striated part by a distinct boundary line. After the formation of the daughter-nuclei, each pole-corpuscle, with its surrounding attraction-sphere, is described as undergoing division and remaining within the daughter-cell as a double system of spheres, ready to initiate the further division of the nuclei which have just been formed. If this be so the attraction-spheres are not to be regarded as developed only during karyokinesis but as forming a prior constituent of the cell, merely becoming more evident at the time of cell-division, and along with the achromatic spindle, which subsequently unites them, may be regarded as initiating and directing the division of the nucleus

Fig. 220.—Stages in the division of the nucleus of a living epithelium cell in the epidermis of a salamander-larva. (Flemming.)

a, cell showing the nucleus transformed into a mass of contorted filaments (corresponds to *b* and *c* of fig. 211); *b*, the nuclear filaments have become fewer and more united, and begin to assume a converging arrangement (compare *d*, *e*, *f*, of fig. 211); *c*, stellate form (compare *g*, fig. 211); *d*, *e*, hour-glass contraction of the nucleus which gradually passes off and the form *c* is resumed. This may occur more than once: eventually the filaments accumulate in a direction parallel to one another near the centre of the cell, and then gradually separate into two sets as shown in *f* (*i*, *j*, *k* in fig. 211). These as they retire towards the poles gradually resume the stellate form *g* (*l*, fig. 211). The time occupied whilst the stages above represented were passed through was about three hours.

and of the cell. In the resting condition of the cell the attraction-sphere and central particle are single, but they undergo division at the commencement of karyokinesis (Boveri). Attraction-spheres and pole-corpuscles have also been described by Flemming in the white blood-corpuscle, and are probably of constant occurrence.

The karyokinetic process has been watched in actual progress in all its stages by more than one observer. The time occupied varies in different animals from half an hour to three hours. Observed thus in the living cell (fig. 220) it is not possible to follow out all the details of the process, which have only been elucidated in tissues the cells of which have been fixed by appropriate hardening reagents and afterwards stained.

The number of the chromatin filaments or chromosomes varies in different animal- and plant-cells from 2 (Ascaris megalocephala) to 24 (Salamandra maculosa) or more. It is probably constant, or nearly so, in the same species, but may be very different even in allied species. In the division of the spermatogenic cells of the testicle to form the spermatoblasts or young spermatozoa, the final separation of the chromosomes into the daughter-nuclei takes place without the occurrence of a corresponding longitudinal cleavage; the result of this is that the spermatoblasts

contain only half the usual number of chromosomes, consequently the male pronucleus, which is formed from the nucleus of the spermatoblast (head of the spermatozoon), also is formed by one half the usual number. The same is the case with the female pronucleus which has parted with one half its total number of chromosomes in extruding the second directive corpuscle, so that the blending of the male and female pronuclei restores to the ovum its full number of chromosomes, and since in the division of this and in all subsequent processes of division, the chromosomes split and pass half into the one and half into the other daughter-nucleus, the number of chromosomes is constant for all the resulting cells of the organism.

The two daughter-cells are each at first smaller than the mother-cell, but they soon grow, and the process may recommence and be repeated in them, and in this way cell-multiplication may be exceedingly rapid. The cells, as is most generally the case, may become entirely separated, but in some cases they remain in partial

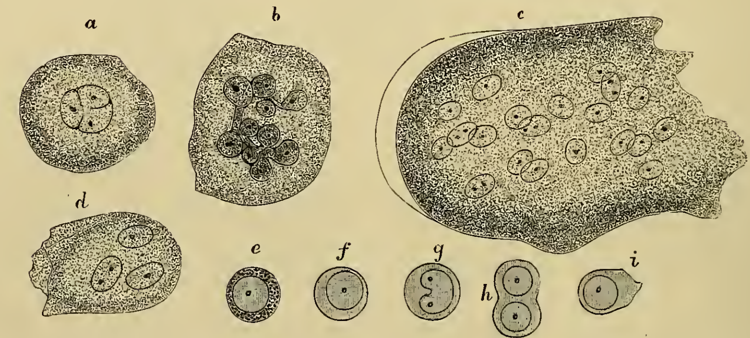


Fig. 221.—Multinucleated cells from the marrow. Highly magnified. (E.A.S.)

a, a large cell the nucleus of which appears to be partly divided into three by constrictions; *b*, a cell the enlarged nucleus of which shows an appearance of being constricted into a number of smaller nuclei; *c*, a so-called giant-cell with many nuclei; *d*, a smaller cell with three nuclei; *e*—*i*, other cells of the marrow.

conjunction, united by filaments of protoplasm which vary in number, length, and thickness.

Sometimes, a multiplication of nuclei within a cell occurs without immediate separation into new cells, as in the large cells which are found in the medullary cavities of bone (fig. 221).

Instances have been observed out of the body in which the amœboid movements of the protoplasm seem to have produced cell-division (Klein, Ranvier), but this occurrence is seldom, and most likely abnormal; indeed, it is found, as a general rule, that whilst cell-division is proceeding, the external manifestations of activity of cell-protoplasm cease almost entirely.

The following are the more important phases of change of the chromoplasmic filaments put in tabular form :—

Network or Reticulum......	1.	Resting condition of mother-nucleus.
Skein or Spirem	2.	Close skein of fine convoluted filaments.
	3.	Open skein of thicker filaments. Achromatic spindle seen within nucleus.
Cleavage	4.	Movement towards middle of nucleus, and cleavage of filaments (which are usually V-shaped).
Star or Monaster	5.	Stellate arrangement of V-filaments in equator of spindle.
Divergence or Metakinesis	6.	Separation of cleft filaments, and movement along fibres of spindle.
Double Star or Dyaster...	7.	Conveyance of V-filaments towards poles of spindle.

DOUBLE SKEIN OR DISPIREM · { 8. Open skein in daughter nuclei.
9. Close skein in daughter nuclei.
NETWORK OR RETICULUM ... 10. Resting condition of daughter nuclei.

Historical.[1]—The existence of utricles or saccules enclosed by a membrane was recognized in the tissues of plants as long ago as the latter half of the 17th century (by Hooke, Malpighi, Grew, and Leeuwenhoek), and a nucleus was noticed and described by Fontana about a century later. At the beginning of the present century, the cellular constitution of plants was further studied and described by Mirbel and Turpin ; but it was not until the third decade of the century that the improvements which had taken place in the microscope led to the general recognition of the fact that, amongst plants at least, the higher organisms are entirely composed of cells, each of which is essentially formed of a membrane enclosing cell-contents and contains a nucleus (R. Brown, Schleiden, 1831—1838). This generalization was extended to the animal tissues by Schwann, in a remarkable work published in German in 1839 (Microscopical Researches into the Accordance in the Structure and Growth of Animals and Plants. Sydenham Society's Translation, 1847), in which he further showed that in all probability every cell is derived from a pre-existing cell.

The researches of Schwann were so widely extended and the evidence he adduced was so conclusive that his ideas, under the name of the "cell-theory" still remain as the accepted doctrine of the constitution of plant and animal organisms. The term *protoplasm* was applied by Purkinje to the substance of animal cells in 1840, but first came into extensive use after its employment by v. Mohl, in 1846, who applied it to the living substance of the plant-cell. The material itself, with all its most prominent characteristics as displayed in Infusoria, was however described, in 1835, under the name of "sarcode," by Dujardin, the accuracy of whose description has, it will be seen, left but little for subsequent observers to add :—"I propose to name *sarcode* that which other observers have termed a living jelly, a substance glutinous, diaphanous, homogeneous, refracting light a little more than water, but much less than oil, extensible and ropy like mucus, elastic and contractile, susceptible of spontaneously forming within itself spherical cavities or vacuoles which become occupied by the surrounding liquid . . . . . . Sarcode is insoluble in water, but is eventually decomposed by it, leaving a granular residuum. Potash does not dissolve it suddenly like mucus or albumen, and seems simply to hasten its decomposition by water ; nitric acid and alcohol immediately coagulate it and render it white and opaque . . . . . . The most simple animals, such as amœbæ and monads, are entirely composed, at least to all appearance, of this living jelly. In higher infusoria it is enclosed in a loose integument which looks like a network on its surface . . . . . . Sarcode is found in ova, zoophytes, worms, and in other animals ; but it is here capable of assuming with age a degree of organization more complex than in animals at the bottom of the scale . . . . . . Sarcode is without visible organs and has no appearance of cellularity ; but it is nevertheless organized, for it emits various prolongations along which granules pass and which are alternately extended and retracted : in one word, it possesses 'life.'"

Gradually, both in plants as well as in the lower animals, it came to be generally recognized that the sarcode of Dujardin and the protoplasm of v. Mohl are endowed with similar attributes, and a cell was defined as composed of structureless protoplasm, endowed with irritability and contractility, containing a nucleus and enclosed by a cell-membrane. That a cell-membrane is, however, not an essential character and is often absent, especially in animal cells, was shown by Leydig (in 1856), and was especially emphasized by M. Schultze and by Brücke (in 1861). Even at the present time the definition of a cell proposed by Leydig still holds good—"a mass of protoplasm furnished with a nucleus."

Up to 1865 protoplasm was universally held to be homogeneous and structureless. Attention was drawn by Frommann, however, to a fibrillar structure in the protoplasm of many cells, and such structure was regarded by him as of universal occurrence. This view was somewhat later expanded by Heitzmann, Klein, and others, who described a reticular structure as occurring in all protoplasm, but it was by no means certain that the structure described might not have been produced by the reagents which were employed to exhibit it ; for it must be borne in mind that precisely such a reticulum as is exhibited in protoplasm which has been treated with alcohol or chromic acid can be equally well produced in solutions containing albumen or mucus. Nevertheless, it is the opinion of many histologists at the present day who have given special attention to the subject (Leydig, Kupffer, Flemming, Carnoy) that protoplasm invariably contains a reticulum, although others, and probably a smaller number, still regard the reticular or spongy structure as non-essential to its constitution (Kollmann, Strasburger, Schwartz). The reticular structure of the nucleus, although it had been previously described by various observers, was for the most part regarded as merely a localized and specialized part of the general cell-reticulum. The existence and

[1] The following account is mainly derived from the "Histoire de la Cellule," given by Carnoy (Biologie Cellulaire, Fascicule 1, 1884).

independence of the nuclear network, and the distinction of the nuclear substance with chromatic and achromatic material was demonstrated by Flemming in 1879. The changes which are characteristic of karyokinesis have since been studied and described by Strasburger and others in plants, by Flemming, Klein, Arnold, Rabl, Carnoy, v. Beneden, Boveri, and many others in animal cells.[1]

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[1] For a full account of the history of the more recent researches on the structure of cells and nuclei at rest and during division, the student is referred to the paper by Waldeyer before mentioned.

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THE EPITHELIAL TISSUES.

An epithelium is a tissue which is composed entirely of cells with a comparatively small amount of intercellular substance. It usually takes the form of a membrane covering the free surfaces of the body. Thus it is well known, that when the skin is blistered, a thin, and nearly transparent membrane, named the cuticle or epidermis, is raised from its surface. In like manner a transparent film, similar in nature to the epidermis, may be raised from the lining membrane of the lips and mouth, in which situation it first received the name of "epithelium;" and under the latter appellation, a coating of the same kind exists on nearly all free surfaces and membranes of the body.[1]

The following are the most important situations in which a covering or lining of epithelial tissue is found: viz., 1. On the surface of the skin. 2. On mucous membranes; a class of membranes to be afterwards described, which line those internal cavities and passages of the body that open exteriorly,—viz., the alimentary canal, the lachrymal, nasal, tympanic, respiratory, urinary, and genital passages; as well as the various glandular recesses and ducts of glands, which open into these passages or upon the surface of the skin.[2] 3. Lining the ventricles of the brain and the central canal of the spinal cord. 4. In the organs of special sense where the cells are often greatly modified and receive the endings of the nerves of special sense. 5. On the inner or free surface of serous membranes, which line the walls of closed cavities in the chest, abdomen, and other parts, and on the inner surface of the heart, blood-vessels and lymphatics. In these situations the epithelial lining has received the name of *endothelium* (His).

In many parts of the connective tissue the cells of that tissue are flattened out and arranged close together, edge to edge, in such a manner as to form a membrane of cells, which so far would come under the definition of the term epithelium. But the cells in question exhibit every transition to the other cells of the connective tissue, so that their enumeration under epithelium would create an artificial separation between cells of the same elementary tissue. They may, however, be conveniently described as epithelium-like (epithelioid). Many histologists are of opinion that a similar distinction should be made for the epithelium of the serous membranes and of the vessels, because these are developed within the mesoblast, and it is the following up of this idea which has led to the adoption of the word "endothelium" to express an epithelium so derived. But, if every epithelium which originates in the mesoblast is to be so designated, we shall be compelled to separate from the other epithelial tissues, with which they are in every way closely allied, the epithelia of the renal, and of the generative organs, since these appear to be derived from the same layer of cells. And indeed, since it has been shown in several instances amongst both invertebrates and vertebrates, that the epithelium of the serous cavities, and even that of the heart, is directly derived from an undoubtedly epithelial layer—the entoderm—it is probable that this is the original and typical mode of origin of all the so-called endothelia, although it has become obscured in the development of higher vertebrates.

Structure of epithelial tissue in general.—Every epithelial tissue is formed entirely of cells united together by cohesive matter, often in too small quantity to be apparent without the employment of nitrate of silver staining. The layer or layers thus formed take the shape of the surface to which they are applied, following accurately all its eminences and depressions. As a rule no blood-vessels

[1] The term "epithelia," which has passed into "epithelium," was introduced by Ruysch to designate the cuticular covering on the red part of the lips. The word "epidermis" he considered inappropriate, as the subjacent surface is not skin (*derma*); but, as it is beset with papillæ, he named the covering layer "epi-thelia," from επι and θηλη, a nipple or papilla. The use of the term has, by a not unusual license been extended so as to signify the same kind of coating when it spreads over non-papillary surfaces.

[2] The hairs and nails and the enamel of the teeth, as the study of their development shows, are also undoubtedly of epithelial origin, but in the case of the enamel and in a lesser degree of the hairs, they have become so specialized that their epithelial structure is scarcely longer recognizable.

penetrate into epithelial tissue, although in some cases minute channels may exist between the cells into which the plasma of the blood, derived from the blood-vessels of the subjacent connective tissue, may pass for the nutrition of the epithelium-cells.

Nerves are abundant in many epithelia, the nervous fibrils passing in the form of fine varicose filaments among the epithelium-cells.

In certain situations branched "migratory cells" which may contain pigment lie in the intercellular substance of an epithelium.

Epithelium-cells vary in structure as well as in shape, and some of these differences will be mentioned in speaking of the varieties of epithelium. The nucleus varies, however, far less than the rest of the cell: in most cases it has an intranuclear network and one or more nucleoli. In the division of epithelium-cells, it undergoes the changes which have already been described.

Classification of epithelia.—The varieties of epithelium may be classified in various ways, but none perhaps are altogether satisfactory. Thus we may distinguish an epithelium according to its origin, as epiblastic, mesoblastic, or hypoblastic, and this distinction is partially indicated when a separate term (endothelium) is used to denote mesoblastic epithelium. Or again, the epithelia may be classed according to their function, and in this way we distinguish between the protective, the secreting, the ciliated, and the sense-epithelia. But without failing to recognize that these modes of classification have a certain amount of importance, it will be most convenient here to follow the prevalent custom, and to classify the varieties of epithelium-cells according to their shape and arrangement.

In the first place we may distinguish an epithelium which is composed of only a single layer of cells as a *simple* epithelium in contra-distinction to a *stratified* epithelium, in which the layers of cells are numerous. Where, on the other hand, the cells are in more than a single layer, but the two or three layers dove-tail the one into the other, so that the structure is not distinctly stratified, the term *transitional* may be employed.

Stratified epithelium.—In a stratified epithelium the cells are disposed in a number of layers, and it is commonly found that the constituent cells of the various strata exhibit every variety of shape. As a rule the cells of the deepest or

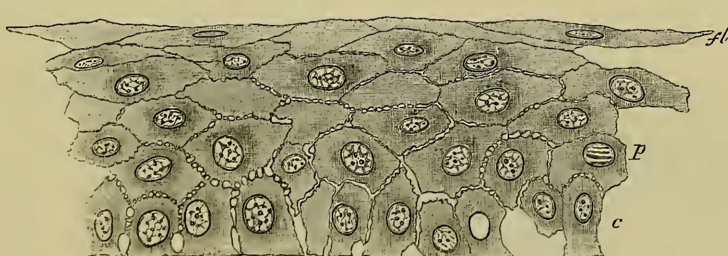


Fig. 222.—Section of the stratified epithelium covering the front of the cornea of the eye. Highly magnified. (E. A. S.)

c, lowermost columnar cells; *p*, polygonal cells above these; *fl*, flattened cells near the surface. The intercellular channels bridged by minute processes of the cell, are well seen. The lower part of the section on the right is somewhat broken.

attached layer are columnar (fig. 222, *c*), and the superficial cells are flattened scales (fig. 222, *fl*) which may be of considerable size, but which do not, like the cells of pavement or simple scaly epithelium, fit together by their edges, but, on the contrary, overlap one another (fig. 223). The cells of the layers immediately external to the columnar layer are rounded in shape or at least only so far modified as to enable them to fit to the columnar cells and to one another (fig. 222, *p*); but as we trace the strata

towards the surface, we find the component cells becoming more flattened and larger, whilst at the same time undergoing a change in their chemical constitution, so that at first the external part, and afterwards the whole of the protoplasm of the cell, is converted into horny substance, even the nucleus being at last involved.

The conversion into horny substance is in many instances preceded by the deposit of a granular material within the cells, which is termed *eleidin* (Ranvier) or *keratohyalin* (Waldeyer). In the epidermis and some other parts the cells which contain this granular material form an almost complete layer between the soft, still protoplasmic, deeper cells and the superficial horny stratum (fig. 224). The layer is termed *stratum granulosum* and was described by Langerhans.

The deeper protoplasmic cells of a stratified epithelium are continually multiplying by cell-division, and, as the new cells which are thus produced in the deeper parts increase in size, they compress and push outwards those previously formed. In this way cells which were at first deeply seated, become gradually shifted towards the surface, undergoing meanwhile the chemical change above spoken of. The older superficial cells are continually being removed by abrasion, while others rise up to supply their place.

Intercellular bridges and channels.—The deeper layers of a stratified epithelium are not closely applied to one another by their edges, but there exists a system of intercellular channels, which are bridged across by fibres which run from one cell to the other (see figs. 222, 224). When the cells are isolated, the fibres are

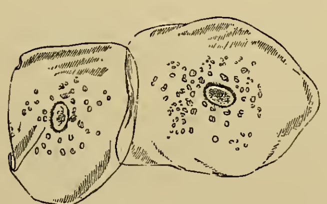


Fig. 223.—Epithelium-scales from the inside of the mouth ; magnified 260 diameters. (Henle.)

Fig. 224.—Portion of epidermis from a section of the skin of the finger, coloured with picrocarmine. (Ranvier.)

a horny layer ; *b*, its deepest part (stratum lucidum) with flakes of eleidin ; *c*, eleidin granules in cells of stratum granulosum ; *d*, deeper cells of stratum mucosum with intercellular channels ; *e*, dentations by which the deepest cells are fixed to the surface of the cutis vera.

broken through and appear as spikes or dentations on the surface and edges of the cells (fig. 225). Sometimes the intercellular channels become widened in consequence of an excess of fluid accumulating in them, but usually they are very narrow and but little obvious.

The spikes and ridges upon the deeper cells of a stratified epithelium were first noticed by Max Schultze, who was of opinion that they were for the purpose of effecting, by indenting with those on adjoining cells, a firmer connexion between the cells of the epithelium. The true relations of the structures in question, and the intercellular channels which are bridged across by them, were discovered by Bizzozero. The researches of J. Arnold and of Thoma have shown that similar intercellular channels occur extensively in all varieties of epithelium. The fibrils which bridge across the intercellular spaces are described by Ranvier as passing

through the protoplasm of the cells. According to Ramón y Cajal, they are covered by a prolongation of cell-membrane. A similar view is taken by Ide, who describes the cell-membrane as reticulated. A radiating system of fibrils has also been shown to occur in the flattened epithelium cells which cover the posterior surface of the cornea, and in this case also the fibrils traverse the intercellular spaces, passing from one cell into another.

Stratified scaly epithelium occurs in one of its simplest and most typical forms covering the anterior surface of the cornea of the eye (fig. 222). It is found also lining the mouth, the chief part of the pharynx, and the œsophagus, and in the female it lines the vagina and part of the cervix uteri, but its most extensive distribution is over the surface of the skin, where it forms the epidermis. In many parts of the epidermis the layers become very numerous, and their arrangement somewhat complicated, as will be noticed in the description of the skin. It may be remarked that, in most of the situations where it is found, stratified scaly epithelium is of epiblastic origin, but this is by no means invariably the case and its occurrence depends much more upon the physiological conditions of the parts which it covers. Thus, wherever a surface is liable to undergo friction or abrasion, there we find a development of stratified scaly epithelium.

Fig. 225.—Two "prickle-cells" from the deeper part of the epidermis. (Ranvier.)

d, space around the nucleus, probably caused by shrinking of the latter.

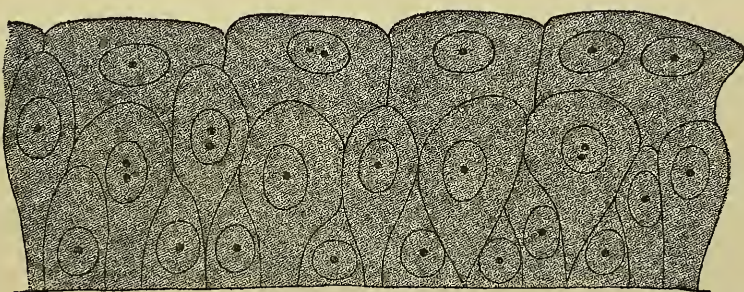


Fig. 226.—Section of the transitional epithelium lining the bladder. (E. A. S.)

a, superficial; *b*, intermediate; and *c*, deep layer of cells.

Transitional epithelium.—Epithelium to which the term transitional may be applied, as being in a sense intermediate between those forms which consist of but a single layer of cells and the stratified which we have just described, may be classed under the three heads of columnar, ciliated, and scaly transitional, according to the kind of cell in each which happens to be most prominent or superficial. The

Fig. 227.—Epithelial cells from the bladder of the rabbit. Highly magnified. (Klein.)

a, large flattened cell from the superficial layer, with two nuclei, and with strongly marked ridges and intervening depressions on its under surface; *a′*, one of the same cells shown in profile; *b*, pear-shaped cell of the second layer showing the manner in which it is adapted to a depression on the superficial cell.

columnar and ciliated transitional epithelia differ, however, so very slightly from the corresponding simple epithelia—viz., merely in the presence between the fixed ends of the columnar and ciliated cells of smaller and probably younger epithelium cells irregularly disposed—that they do not seem to merit any special description. But the scaly transitional epithelium which is met with lining the urinary bladder and ureters presents several peculiarities. It consists of three or four layers of cells, of which the inner or most superficial are large flattened scales when examined from the distended bladder (fig. 227, *a*); almost cubical in shape when taken from the collapsed organ; smooth over their free surface, but pitted on the opposite side, being moulded over the rounded ends of the cells which form the next layer. These are pyriform, and the smaller end of the pear is set upon the subjacent connective tissue, whilst the larger end has the position just mentioned (fig. 227). Filling up the intervals between these tapering cells are the smaller irregular cells of the third layer (fig. 226, *c*). All these cells have distinct nuclei, and in the flattened superficial cells two nuclei may often be seen in the cell. If this is an indication that the cell is about to divide, the mode of growth of this kind of epithelium must be different from that of the stratified scaly variety, in which the multiplication of the cells appears to take place exclusively in the deeper layers.

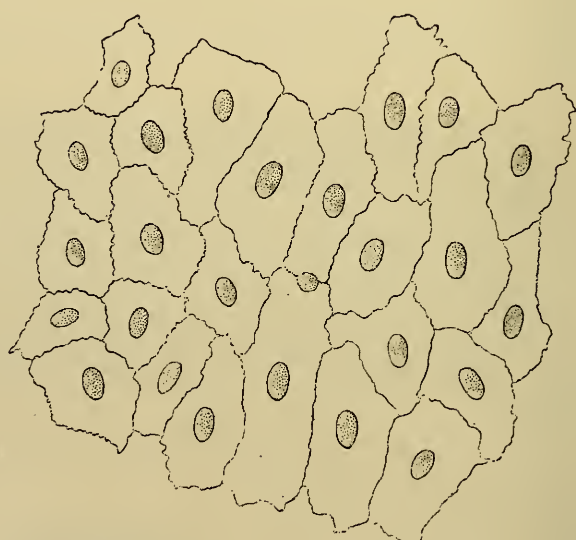


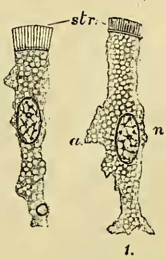
Fig. 228.—Pavement epithelium, scraped from a serous membrane. *a*, cell-body; *b*, nucleus; *c*, nucleoli. (Henle.)

Fig. 229.—Pavement epithelium (endothelium) from the omentum of the rabbit. Nitrate of silver staining. (E. A. S.)

Pavement epithelium.—In this the cells form polygonal plates or scales, which fit together by their edges like the tiles of a mosaic pavement. The lines of junction of the cells may be straight, or they may be more or less jagged or sinuous. The flattened mesoblastic epithelia (endothelia), such as the epithelium of serous membranes and of the vessels and that lining the anterior chamber of the eye belong to this variety, but it includes also the epithelium lining the alveoli of the lungs which is of hypoblastic origin; that covering the outer surface of the membrana tympani, and that lining the mammary ducts, both of which are epiblastic.

Columnar epithelium.—A second variety of simple epithelium is the *columnar*,

or *cylinder-epithelium*, in which the cells have a prismatic figure, and are set upright on the surface which they cover. In profile a row of these cells looks for the most part like a close palisade (fig. 231); but viewed from the surface each cell has a polygonal outline, the cells being flattened where they touch, from mutual com-



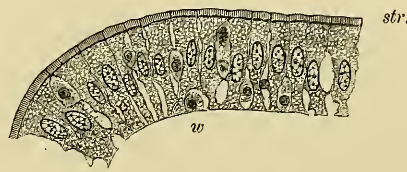


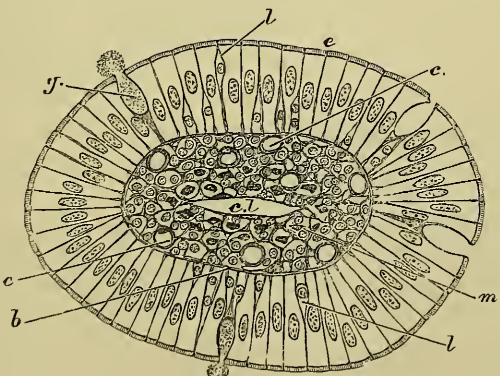
Fig. 230.—Columnar epithelium cells of the rabbit's intestine. (E. A. S.)

The cells have been isolated after maceration in very weak chromic acid. The protoplasm is reticular and vacuolated; the striated border (*str.*) is well seen, and the bright disc separating this from the cell-protoplasm; *n*, nucleus with intranuclear network; *a*, a thinned out wing-like projection of the cell which probably fitted between two adjacent cells.

Fig. 231.—A row of columnar cells from an intestinal villus of the rabbit. (E. A. S.)

str, striated border; *w*, wander-cells between the epithelium cells.

pression, so that thus again a mosaic pattern is produced. Columnar epithelium-cells vary much in form, in dimensions, and even in structure. Those which may be looked upon as typical are of a long tapering figure, the finer extremity being set



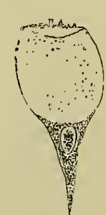


Fig. 232.—Cross-section of a villus of the intestine. (E. A. S.)

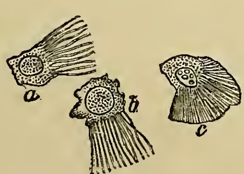
e, columnar epithelium with striated border; *g*, goblet cell, with its mucus partly extended; *l*, lymph-corpuscles between the epithelium-cells; *b*, basement membrane; *c*, sections of blood capillaries; *m*, section of plain muscular fibres; *c. l.*, central lacteal.

Fig. 233.—Goblet-cell from trachea. Highly magnified. (Klein.)

upon a surface, and the other and larger end being free. At their sides and edges the columnar cells are often irregular and jagged, especially where, as is often the case, lymphoid or wander-cells are met with between the epithelium-cells (fig. 231, *w*). Indeed the cells are not by any means so regular in shape as they are often figured, being often compressed laterally, and sometimes extended sideways into flattened lamellæ (fig. 230, *a*), which fit between the adjacent cells of the epithe-

lium. There is always a distinct oval nucleus which contains a network of chromatoplasm. The nucleus may cause a bulging in the part of the cell in which it is situated, and the nuclei of adjacent cells are on this account often seated in different planes. The substance of the cell usually appears granular, but on closer inspection with higher powers it may be seen that the granular appearance is caused by vacuolation and reticulation of the protoplasm. The cell may contain fatty globules and other substances, among which the most deserving of mention is mucin, the chief organic constituent of mucus. The mucin (or mucigen) usually takes the form of a granular deposit within the cell, especially in the part nearest the free border ; when fully formed the granules swell, and their substance escapes in the form of mucus ; the nucleus is often pressed down towards the finer extremity of the cell. Columnar epithelium cells which are thus altered by distension of the outer or free part of the cell by mucus are termed from their shape " goblet or chalice cells " (figs. 232, 233).

In typical columnar epithelium cells, such as those lining the mucous membrane of the small intestine, the free border differs from the rest of the cell in being more refracting and finely striated. This *striated border* of the cell (figs. 230 and 231, *str.*) is often spoken of as the cuticular layer, and it is thereby assumed that it is composed of



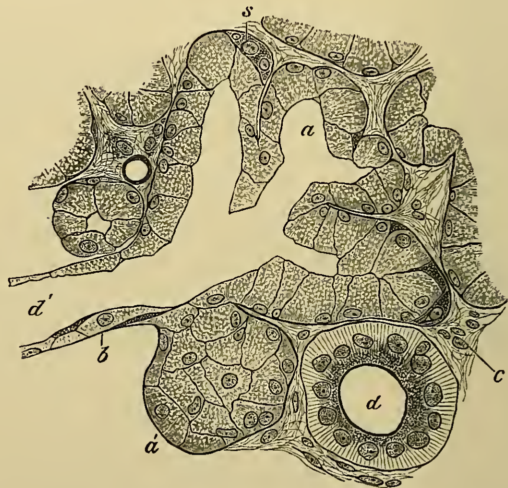


Fig. 234.—Isolated cells from the convoluted tubules of the rat's kidney. (Heidenhain).

Fig. 235.—Section of a racemose gland, showing the commencement of a duct in the alveoli. Magnified 425 diameters. (E. A. S.)

a, one of the alveoli, several of which are in the section shown grouped around the commencement of the duct, *d'* ; *a'*, an alveolus, not opened by the section ; *b*, basement membrane in section ; *c*, interstitial connective tissue of the gland ; *d*, section of a duct which has passed away from its alveoli, and is now lined with characteristically-striated columnar cells ; *s*, semilunar group of darkly-stained cells at the periphery of an alveolus.

something different from the cell-protoplasm. The border does not however, appear to offer a greater resistance than does the cell-protoplasm to the action of reagents, for those which destroy the protoplasm of the cell destroy also the striated border. After having been hardened by reagents it may be detached from the rest of the cell, and since the striated free borders of adjacent cells often adhere together, a continuous membrane may thus be obtained, marked by a mosaic of fine lines indicating the division between the cells from which this " cuticula " has become detached. The fine striæ appear to be caused by the existence of fibrils or septa (perhaps spongioplasmic). The striated cuticula is not immediately in contact with the protoplasm of the cell, but is separated from it by a thin disk composed of a substance which refracts the light even more than the striated border. This disk (shown in fig. 230) corresponds in situation to the bright border of the ciliated epithelium cells (see below), and it is possible that the striated border is the morphological equivalent of the bunch of cilia upon those cells. Columnar epithe-

lium-cells are met with in their most characteristic form lining the mucous membrane of the intestines.

Some columnar epithelium-cells are very long, others very short, so as to look cubical when seen in profile. They vary in form, moreover, according to the shape of the surface which they cover, thus they may be larger at the base than at the free end, as when they line a tube or duct, and in a section of this they then appear wedge-shaped.

Some epithelium cells, which must be reckoned in with this variety, have a peculiar striated aspect in the basal or fixed half of the cell. This is the case with the cells which line the smaller ducts of the salivary glands and some of the tubules of the kidney (fig. 234 and fig. 235, *d*).

In the human subject, columnar epithelium is chiefly, but by no means exclusively, derived from the hypoblast.

Glandular epithelium.—This variety of epithelium is chiefly characteristic of the terminal recesses or alveoli of secreting glands. In form the cells are columnar, cubical, polyhedral or spheroidal, and are usually set round a tubular or saccular cavity, into which the secretion is poured (fig. 235, *a*). The protoplasm of the cells is generally occupied by the materials which the gland secretes. This epithelium will be more fully described in the chapter on secreting glands.

Ciliated epithelium.—In this form of epithelium, the cells, which are generally columnar, bear at their free extremities little hair-like processes, which are agitated incessantly during life, and for some time after systemic death, with a lashing or vibrating motion. These minute and delicate moving organs are named *cilia*. They exist very extensively throughout the animal kingdom; and the movements which they produce are subservient to very varied purposes in the animal economy.

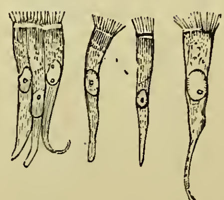


Fig. 236.—Columnar ciliated epithelium cells from the human nasal membrane; magnified 300 diameters. (Sharpey.)

Distribution and use.—In the human body ciliated epithelium occurs in the following parts, viz:—1. On the mucous membrane of the air-passages and its prolongations. It commences at a little distance within the nostrils, covers the membrane of the nose (except the proper olfactory part) and of the adjoining bony sinuses, and extends up into the nasal duct and lachrymal sac. From the nose it spreads backwards a certain way on the upper surface of the soft palate, and over the upper or nasal region of the pharynx; thence along the Eustachian tube and lining membrane of the tympanum, of which it covers the greater part. The lower part of the pharynx is covered by scaly epithelium; but the ciliated epithelium begins again in the larynx a little above the glottis, and continues throughout the trachea and the bronchial tubes in the lungs to their smallest ramifications. Over the vocal cords, however, the epithelium is of the stratified scaly variety. 2. On the mucous lining and in the glands of the body of the uterus and extending along the Fallopian tubes, even to the peritoneal surface of the latter at their fimbriated extremities. 3. In the testicle lining the vasa efferentia, coni vasculosi, and first part of the tube of the epididymis. 4. Lining the ventricles of the brain, except the fifth ventricle, and throughout the central canal of the spinal cord. 5. In the excretory ducts of certain small racemose glands of various parts (tongue, pharynx, &c.) 6. In the embryo, lining the œsophagus and parts of the stomach and extending also over the whole of the pharynx.[1]

[1] Cilia have also been described in some mammals at the commencement of the tubules of the kidney (Klein), a situation where in lower vertebrates they have long been known to exist.

In other mammiferous animals, as far as examined, cilia have been found in nearly the same parts. To see them in motion, a portion of epithelium may be scraped off any ciliated mucous membrane and examined in a drop of weak solution of salt (0·6 per cent.) or serum of blood. When it is now viewed with a magnifying power of 200 diameters or upwards, a very obvious agitation will be perceived at the edge of the detached piece of epithelium ; this appearance is caused by the moving cilia, with which the surface of the membrane is covered. Being set close together, and moving simultaneously or in quick succession, the cilia, when in brisk action, give rise to the appearance of a bright transparent fringe along the margin of the membrane, agitated by such a rapid and incessant motion, that the single threads which compose it cannot be perceived. The motion here meant, is that of the cilia themselves ; but they also set in motion the adjoining fluid, driving it along the ciliated surface, as is indicated by the agitation of any little particles that may accidentally float in it. The fact of the conveyance of fluids and other matters along the ciliated surface, as well as the direction in which they are impelled, may also be made manifest by immersing the membrane in fluid, and dropping on it some finely-pulverised substance (such as charcoal in fine powder), which will be slowly but steadily carried along in a constant and determinate direction ; and this may be seen with the naked eye, or with the aid of a lens of low power (Sharpey).

Cilia have been shown to exist in almost every class of animals, from the highest to the lowest.[1] The immediate purpose which they serve is, to impel matter, generally more or less fluid, along the surfaces on which they are attached ; or, to propel through a liquid medium the ciliated bodies of minute animals, or other small objects which are provided with cilia ; as is the case with many infusorial animalcules, in which the cilia serve as organs of locomotion like the fins of larger aquatic animals. In many of the lower tribes of aquatic animals, cilia acquire a high degree of importance : producing the flow of water over the surface of their organs of respiration, indispensable to the exercise of that function ; enabling the animals to seize their prey, or swallow their food, and performing various other offices of greater or less importance in their economy. In man and the warm-blooded animals, their use is apparently to impel secreted fluids or other matters along the ciliated surface, as, for example, the mucus of the wind-pipe and nasal sinuses, which they carry towards the outlet of these cavities.

Structure.—The cells of a ciliated epithelium contain oval nuclei, exhibiting for the most part a distinct intra-nuclear network, and one or more bright nucleoli. Viewed with a moderate magnifying power, their protoplasm looks granular, although the free border of the cell through which the cilia pass presents a clear aspect (fig. 236). The cells have most generally an elongated form, like the particles of the columnar epithelium, which they resemble too in arrangement, but they are often of greater length and more pointed at their lower end ; and this is not unfrequently irregularly forked in those parts where a deeper layer of cells exists below the ciliated cells (fig. 237). The cilia are attached to their broad or superficial end, each cell bearing a tuft of these minute hair-like processes. In some cases, the cells are shorter and cubical in figure, and when completely detached may appear spheroidal.

It has been shown by Engelmann that in large ciliated cells (fig. 238) such as those which line the alimentary canal of some mollusks, e.g., the mussel and oyster, it is possible to make out that the highly refracting free border of the cell to which the cilia are attached is in reality formed of a number of small juxtaposed fusiform or cylindrical knobs (*basal knobs*). To each of these a cilium is attached on the one side, and from the other end there passes towards the end of the cell a fine,

[1] The Arthropoda offer a singular exception, and it is remarkable that in many of them the spermatozoa are also devoid of a vibratile filament.

varicose filament; these filaments are termed by Engelmann the *rootlets* of the cilia. They approach one another as they traverse the length of the cell, and may be united towards the extremity into a single thread. They are not connected with the nucleus. The cilia are attached to the basal knobs, each one by a somewhat narrowed portion or neck (*intermediate segment* of Engelmann). It is here that the cilia usually break off from the cell (see fig. 238). Beyond the neck the cilium swells out into a small bulbous enlargement, and from this the shaft tapers gradually to its extremity. The rootlets, as well as the cilia themselves, are said by Engelmann to be doubly refracting (anisotropous), whereas the basal knob

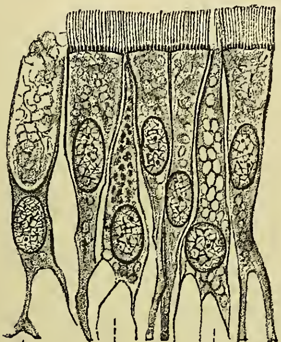


Fig. 237.—CILIATED EPITHELIUM CELLS FROM THE TRACHEA OF THE RABBIT; HIGHLY MAGNIFIED, (E. A. S.).

m^1, m^2, m^3, mucus-secreting cells, lying between the ciliated cells, and seen in various stages of mucin-formation.

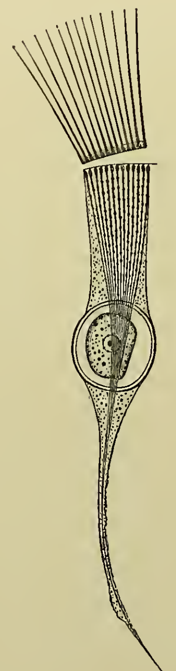


Fig. 238.—A CILIATED EPITHELIUM-CELL OF A MOLLUSK. (Engelmann.)

is isotropous. A similar structure, although less distinct, is also to be made out in ciliated cells from higher animals (frog and mammal).

The columnar ciliated epithelium may exist as a simple layer, as in the uterus and Fallopian tubes, the finest ramifications of the bronchia, and the central canal of the spinal cord and ventricles of the brain; but in various other parts—as the nose, pharynx, Eustachian tube, the trachea and its larger divisions—there is a layer of elongated and irregular cells beneath the superficial ciliated range, filling up the spaces between the pointed and forked extremities of the latter. These cells have been supposed to acquire cilia, and take the place of ciliated cells which are cast off; but this is doubtful, and they appear rather to be concerned with the secretion of mucus, since mucigen occurs within them in all stages of formation, and they become eventually distended by it into goblet-cells (see fig. 237, where the intermediate cells, m^1, m^2, and m^3 show three stages of formation of mucus).

When the ciliated epithelium is artificially removed from a portion of the inner surface of the rabbit's trachea, the denuded surface speedily becomes again covered with epithelium, which grows over it from the edge, but the cells form at first a single layer of flattened epithelium. They next acquire cilia, and afterwards become columnar, the epithelium thus assuming the character which it has normally in that situation.

There is no reason to believe that ciliated epithelium-cells are in connection either with nerve-fibres, or with the cells of the subjacent connective tissue. An anatomical connection with subjacent cells and fibres has been described in reference to the columnar ciliated epithelium of the central canal of the spinal cord and of the Sylvian aqueduct. But this is a most difficult point to determine exactly, and even if such a connection should be proved, the cells in the situations above mentioned are entirely different in many respects from ordinary ciliated cells. They are relatively slender, and their fixed non-ciliated ends pass into branching fibres, which lose themselves in a network which underlies the epithelium, and appears to be formed chiefly, if not entirely, by the interlacement of the ramified cell-processes. These peculiar ciliated cells closely resemble those which constitute the structures known as nerve-epithelia in some of the lower invertebrata, and which in some of these animals represent the whole central nervous system.

The cilia themselves differ widely in size in different animals, nor are they of equal size in all parts of the same animal. In the human windpipe they measure $\frac{1}{4000}$th to $\frac{1}{2500}$th of an inch in length ; but in many invertebrate animals they are much larger than this, and in the human epididymis are from eight to ten times longer than in the trachea.

In figure they have the aspect of slender conical, or slightly flattened filaments ; broader at the base, and usually pointed or rounded at their free extremity. Their substance is transparent, soft and flexible. It is to all appearance homogeneous, and no fibres, granules, or other indications of definite internal structure, have been satisfactorily demonstrated in it.

The flagellum of Noctiluca, which bears a general resemblance to a large cilium and has a similar rhythmic lashing action, is transversely striated, and the cilium or tail of a spermatozoon also shows certain indications of structure, but nothing of the kind has been observed in ordinary cilia.

Nature of ciliary movement and influence of varying conditions and reagents.— If the cilia be detached from the cell they cease to move, and on this account it is thought by some, that the movement is entirely a passive one, caused by movements in the cell-protoplasm acting upon the rootlets of the cilia. But the apparently independent motion of the tails of the spermatozoa, which are comparable to long single cilia, and that of the long cilia which are protruded from many of the lower animal and plant organisms, has led other authorities to believe that the movement is due to the contraction of the cilia themselves.

There is, however, a third mode of explanation of the movements which may be suggested and which would have the advantage of bringing them into close relationship with the amœboid movements of cell-protoplasm, and, as we shall afterwards see, with the process of contraction and extension of muscle. The explanation is briefly as follows :—If we suppose that a cilium is a hollow curved extension of the cell, occupied by hyaloplasm, and invested by a delicate elastic membrane (perhaps an extension of the spongioplasm), then it must follow that if there be a rhythmic flowing of hyaloplasm from the body of the cell, into and out of the cilium, an alternate extension and flexion of that process would thereby be brought about. The same result would be got, supposing the cilium to be a straight and not a curved extension of the cell, if the enveloping membrane were thicker (or otherwise less extensible) along one side than along the other. This last assumption would also enable one the better to account for the spiral direction of the movement of certain cilia ; for this form of movement would be produced if the line of lessened extensibility in these cilia were to pass in a cork-screw fashion along the cilium in place of straight along one side, as assumed for ordinary cilia.

The cilia vibrate with a frequency of not less than ten times in a second when moving actively, but the rate of movement may be much slower than this. The movement of cilia is incessant so long as the cells remain alive, but that of spermatozoa often exhibits intervals of rest alternating with periods of rhythmic movement.

The manner in which cilia move, is best seen when they are not acting very briskly. The motion of an individual cilium may be compared to that of a carter's whip, the cilium being rapidly flexed in one direction, that of the current which they produce, and returning more slowly in the other direction. The motion does not involve the whole ciliated surface at the same moment, but is performed by the cilia in regular succession, giving rise to the appearance of a series of waves travelling along the surface, like the waves caused by the wind in a field of corn. When they are in very rapid action the undulation is less obvious, and, as Henle remarks, their motion then conveys the idea of swiftly-running water. The undulating movement may be beautifully seen on the gills of a mussel. The undulations, with some exceptions seem always to travel in the same direction on the same parts. The impulsion, also, which

the cilia communicate to the fluids or other matters in contact with them, maintains a constant direction ; unless in certain of the lower animals, in which the motion is often variable and arbitrary in direction, and might even be supposed to be voluntary. Thus in the windpipe of mammalia, the mucus is conveyed upwards towards the larynx, and, if a portion of the membrane be detached, matters will still be conveyed along the surface of the separated fragment in the same direction relatively to that surface, as before its separation.

The persistence of the ciliary motion for some time after death, and the regularity with which it goes on in parts separated from the rest of the body, sufficiently prove that, with the possible exceptions alluded to, it is not under the influence of the will of the animal, nor dependent for its production on the nervous centres, and it does not appear to be influenced in any way by stimulation or sudden destruction of these centres. The time during which it continues after death or separation differs in different kinds of animals, and is also materially influenced by temperature and by the nature of the fluid in contact with the surface. In warm-blooded animals the period varies from two or three hours to two days, or even more ; being longer in summer than in the cold of winter. In frogs the motion may continue four or five days after destruction of the brain and spinal cord ; and it has been seen in the gullet of the tortoise fifteen days after decapitation, continuing seven days after the muscles had ceased to be irritable.

Variations of temperature exert a very marked effect upon the rate and vigour of the motion of cilia. Thus, in warm-blooded animals it is altogether stopped if the temperature is lowered to 6°C., whereas, in cold-blooded animals, such as the frog and mussel, it goes on unimpaired at 0°C. The motion which has become quiescent from cold, may be revived by warmth, and becomes more active in proportion to the rise in temperature up to a certain point, which differs in warm and cold-blooded animals. In the former, this maximum temperature is about 45°C. ; above this the movement quickly ceases, the cilia passing into a coagulated stiffened condition, known as heat-rigor, and which, if well marked, is not recovered from. The temperature of the body seems to be that which is most favourable to the action of the cilia ; that is to say, they will, if removed from the body, work vigorously for a longer time at this temperature than at any other.

Cilia will continue to work for a time in the absence of free oxygen. This was shown by Sharpey, who noticed the movement of the cilia upon the gills of the tadpole to proceed for some hours, even when immersed in water which had been deprived of its oxygen by boiling. This experiment shows that like the substance of muscle, the protoplasm of the ciliated epithelium-cell can store up oxygen in a combined form for future use.

The immediate action of water is to increase the activity of cilia. Agents or conditions, on the other hand, which abstract water from the tissue, retard or arrest the action. Thus most of the common acid and saline solutions when concentrated arrest the action of cilia instantaneously in all animals, but dilution delays this effect, and when carried far enough, prevents it altogether. Fresh water soon arrests the motion in marine animals ; but it evidently acts by destroying the epithelium-cells, which in these cases are adapted to a different medium. Even in air-breathing and fresh-water animals water has after a time the same action, provided the ciliated cells are detached, so that it can pass by imbibition into their protoplasm. Solutions of potash or soda, if extremely dilute, act like water, but more powerfully. Virchow observed that a diluted solution of either potash or soda would revive the movement of cilia after it had just ceased. The vapour of chloroform arrests ciliary action, but the motion revives again if the application of the vapour is discontinued (Lister).

Carbonic acid gas resembles chloroform in its action, rapidly arresting the movement if conveyed over a ciliated surface, but the action speedily recommences on again admitting air. The passage of the gas is, however, generally found to stimulate the movement at first.

Bile stops the action of cilia, while blood prolongs it in vertebrated animals ; but the blood or serum of the vertebrata has quite an opposite effect on the cilia of invertebrate animals, arresting their motion almost instantaneously.

It was noticed by Steinbuch that a mechanical stimulus, insufficient to injure the cilia, such as that produced by the impulse of a current of fluid, acts markedly in exciting the activity of ciliary motion.

Electric stimulation, unless it causes injury to the ciliated surface, produces no obvious effect.

Whatever views are entertained concerning the nature and source of the power by which the cilia act, it must be borne in mind that each ciliated cell is individually endowed with the faculty of producing motion, and that it possesses in itself whatever organic apparatus and whatever physical or vital property may be necessary for that end ; for single epithelium cells are seen to exhibit the phenomenon long after they have been completely isolated.

Historical.—Ciliary movement was first noticed (in the mussel) by de Heide in 1683, the movements of spermatozoa having been previously discovered by Ham and Leewenhoek. Subsequently the movements were noticed in various situations. A comprehensive account of the structure, distribution, and mode of action of cilia was given by Sharpey in the article "Cilia," in Todd and Bowman's Cyclopædia. That article, which appeared in 1835, was the result of much laborious investigation, and still forms the basis of our knowledge on the subject.

Simultaneously with Sharpey's article a full description was also given by Purkinje and Valentin, including an account of the discovery of this phenomenon in mammals, birds, and reptiles, and of the literature up to that time (De phænomeno generali et fundamentali motûs vibratorii continui, 1835). The account by Engelmann in his article on Protoplasm and Ciliary movement[1] in Hermann's Handbuch der Physiologie also includes an historical sketch of the subject up to 1879.

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[1] A translation of this article is to be found in the *Quarterly Journal of Microscopical Science*, for 1880.

THE CONNECTIVE TISSUES.

Three principal modifications or varieties of connective tissue have long been recognized and separately described, viz., *areolar tissue, fibrous tissue* and *elastic tissue.* Others, however, belong unmistakeably to the same group, as the study of their structure and the history of their development in the mesoblast clearly show. Of these the most important are *adipose tissue, retiform and lymphoid tissue, cartilage, bone* and the *elements of the blood and lymph.* It will be convenient to study the last-named elements before the structure of the connective tissues proper is considered.

THE BLOOD.

The most striking external character of the blood is its well-known colour, which is bright red approaching to scarlet in the arteries, but of a dark purple or modena tint in the veins. It is a somewhat clammy and consistent liquid, a little heavier than water, its specific gravity being about 1·055 ; it has a saltish taste, a slight alkaline reaction, and a peculiar faint odour.

To the naked eye the blood appears opaque and homogeneous ; but, when examined with the microscope, either while within the minute vessels, or when spread out into a thin layer upon a piece of glass, it is seen to consist of a transparent colourless fluid, named the "lymph of the blood," "liquor sanguinis," or "plasma," and minute solid particles or corpuscles immersed in it. These corpuscles are of two kinds, the coloured and the colourless : the former are by far the more abundant, and have been long known as "the red particles," or "globules," of the blood ; the "colourless," "white," or "pale corpuscles," on the other hand, being fewer in number and less conspicuous, were later in being generally recognised.

When blood is drawn from the vessels, the liquor sanguinis separates into two parts ;—into fibrin, which becomes solid and takes the form of fine interlacing filaments, and a pale yellowish liquid named *serum.*

In a cubic millimeter of healthy human blood there are on an average 5,000,000 red corpuscles (Vierordt) and 10,000 white corpuscles. The number of white corpuscles varies much more than that of the red, and the proportion of the white to the red is variously given at from 1 : 1000 to 1 : 250. There are said to be fewer red corpuscles in the female (4,500,000 in a cubic millimeter according to Welcker).

The numeration of the blood-corpuscles is readily performed. A little blood, obtained by pricking the finger, is measured in a capillary tube, and is then mixed with a measured amount (say 100 times its volume) of dilute solution of sulphate of soda, or some other salt which will maintain its fluidity and at the same time preserve the corpuscles nearly unaltered ; the latter can then be counted in a small known quantity of the mixture. This part of the operation is effected by placing a drop of the mixture in the middle of a glass "cell" of a certain depth (say $\frac{1}{10}$th of a millimeter), the bottom of which is ruled in squares, the sides of which are of a known dimension (say again $\frac{1}{10}$ mill.). If now a covering glass is placed over the cell so as to touch the drop, the latter will form a layer of the mixture $\frac{1}{10}$ mill. deep, and the part above each square will represent a cube of liquid the sides of which measure $\frac{1}{10}$ mill. So that by counting the number of corpuscles in ten squares, after allowing them time to subside, and multiplying the result by 10,000, the number in a cubic millimeter of the blood is obtained.

The methods of Hayem and Nachet, Gowers, and Thoma are based on the above principle. The average results obtained by recent investigators agree closely with the original estimates of Vierordt and Welcker.

RED CORPUSCLES OF THE BLOOD.

These are not spherical, as the name "globules," by which they were formerly designated, would seem to imply, but flattened or disk-shaped. Those of the human blood (fig. 239 and fig. 240, A) have a nearly circular outline, like a piece of coin, and most of them also present a shallow cup-like depression or dimple on both surfaces; their usual figure is, therefore, that of biconcave disks. Their magnitude differs somewhat even in the same drop of blood, and it has been variously assigned by authors; but the prevalent size may be stated at $\frac{1}{3200}$th of an inch (·007 to ·008 millimeter)[1] in diameter, and about one-fourth of that in thickness. A few corpuscles may usually be found which are not more than about one-half this size (microcytes), and others which are rather larger (up to about $\frac{1}{3000}$th of an inch), and

Fig. 239.—Human blood as seen on the warm stage. Magnified about 1000 diameters. (E. A. S.)

r, r, single red corpuscles seen lying flat; r', r', red corpuscles on their edge and viewed in profile; r'', red corpuscles arranged in rouleaux; c, c, crenate red corpuscles; p, a finely granular pale corpuscle; g, a coarsely granular pale corpuscle. Both have two or three distinct vacuoles, and were undergoing changes of shape at the moment of observation; in g, a nucleus also is visible.

every gradation in size between these two extremes may be met with, but the great majority average $\frac{1}{3200}$th of an inch under normal conditions. In some diseases, especially pernicious anæmia, the relative number of microcytes is greatly increased.

In mammiferous animals generally, the red corpuscles are shaped as in man, except in the camel tribe, in which they have an elliptical outline. In birds, reptiles, amphibia, and most fishes, they are oval disks with a central elevation on both surfaces (fig. 240, B, and fig. 245, from the frog), the height and extent of which, as well as the proportionate length and breadth of the oval, vary in different instances, so that in some fishes the elliptical form is almost shortened into a circle.

The size of the corpuscles differs greatly in the different classes of Vertebrata; they are largest in the Amphibia. Thus in the frog they are about $\frac{1}{1000}$th of an inch long and $\frac{1}{1700}$th broad; in Proteus anguineus, $\frac{1}{400}$th of an inch long and $\frac{1}{727}$th broad; in Amphiuma tridactylum, where they are largest, the red corpuscles are one-third larger than those of the Proteus. In birds they range in length from about $\frac{1}{2000}$th to $\frac{1}{1700}$th of an inch. Amongst mammals the elephant has the largest red blood-corpuscles ($\frac{1}{2700}$th of an inch); those of the dog average $\frac{1}{3500}$th of an inch; those of the sheep $\frac{1}{5000}$th of an inch; the goat was long supposed to have the smallest ($\frac{1}{6400}$th of an inch), but Gulliver found them about half this size in the Meminna and Napu deer.

In observations upon the blood of different races of mankind, Richardson found no constant difference, the average diameter of the red blood-corpuscle being $\frac{1}{3224}$th of an inch. The corpuscles of many mammals, and notably the dog among the common domestic animals, approach so nearly in size to the human blood-corpuscles as to be indistinguishable from them.

When viewed singly by transmitted light the coloured corpuscles do not appear red, but merely of a reddish-yellow tinge, or yellowish-green in venous blood. It is

[1] The one-thousandth part of a millimeter is often known as a *micro-millimeter* or *micron*, and is represented by the Greek letter μ. The diameter of a red blood corpuscle is then expressed as 7—8 microns (7μ—8μ).

only when the light traverses a number of corpuscles that a distinct red colour is produced.

In consequence of the biconcave shape of the corpuscle, it looks darker in the middle than at the edge when viewed with only a moderate magnifying power, or at

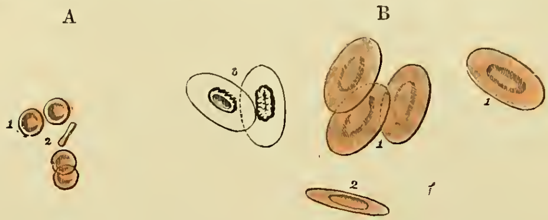

Fig. 240.—HUMAN RED CORPUSCLES (A) AND BLOOD CORPUSCLES OF THE FROG (B) PLACED SIDE BY SIDE TO SHOW RELATIVE SIZE. 500 DIAMETERS.

1, shows their broad surface; 2, one seen edgeways; 3, shows the effect of dilute acetic acid; the nucleus has become distinct (from Wagner).

a distant focus; but the middle of the corpuscle appears lighter than the periphery when a close focus or a very high magnifying power is employed.

The red disks, when blood is drawn from the vessels, sink in the plasma; they have a singular tendency to run together, and to cohere by their broad surfaces, so as to form by their aggregation cylindrical columns, like piles or rouleaus of money, and the rolls or piles themselves join together into an irregular network (figs. 239 and 241). Generally the corpuscles separate on a slight impulse, and they may then unite again. The phenomenon will take place in blood which has been in any way brought to a standstill within the living vessels as well as in blood that has stood for some hours after it has been drawn, and also when the globules are immersed in serum in place of liquor sanguinis.

Fig. 241. — RED CORPUSCLES COLLECTED INTO ROLLS (after Henle).

It has been shown by Norris that disks which float completely immersed in any fluid will, when the fluid comes to rest, tend to adhere together in the form of rouleaus provided that the surface of the disks is of a nature not to be wetted by the fluid in which they float. Thus cork disks which have been weighted so that they neither rise nor sink in water do not adhere together so long as they are freely wetted by the water, but if their surfaces are coated with a thin film of fatty substance the disks tend to run together into rouleaus. As it is probable (see below, Structure of Red Corpuscles) that the red disks do actually possess a superficial film of fatty substance, the facts pointed out by Norris appear to suggest a reasonable explanation of the rouleau-formation which occurs in blood which has been allowed to come to rest.

The human blood-corpuscles, as well as those of the lower animals, often present deviations from the natural shape, which are most probably due to causes acting after the blood has been drawn from the vessels, but in some instances depend upon abnormal conditions previously existing in the blood. Thus, it is not unusual for many of them to appear shrunken and crenated, when exposed under the microscope (fig. 239, *c*, *c*; fig. 242, *f*), and the number of corpuscles so altered often appears to increase during the time of observation. This is, perhaps, the most common change; it occurs whenever the density of the plasma is increased by the addition of a neutral salt, and is one of the first effects of the passage of an electric shock. The corpuscles may become distorted in various other ways, and corrugated on the surface; not unfrequently one of their concave sides is bent out, and they acquire a cup-like figure.

Gulliver made the curious discovery that the corpuscles of the Mexican deer and some allied species present very singular forms, doubtless in consequence of exposure; the figures they assume are various, but most of them become lengthened and pointed at the ends, and then often slightly bent, not unlike caraway-seeds.

Structure of the coloured blood corpuscle.—Each red corpuscle is formed of two parts, a coloured and a colourless, the former being a solution of *hæmoglobin*, the latter, the so-called *stroma*, which is in by far the smaller quantity, being composed of various substances, chief among these being lecithin and cholesterin, together with a small amount of cell-globulin (Halliburton and Friend). Water constitutes about two-thirds of the corpuscles; if the water is driven off, about 90 per cent. of the residue is hæmoglobin.

If water be added to a preparation of blood under the microscope, the water is imbibed and the concave sides of the corpuscle become bulged out so that it is rendered globular. By the further action of the water the hæmoglobin is dissolved

Fig. 242.—*a–e*, successive effects of water upon a red blood-corpuscle; *a*, corpuscle seen edgeways, slightly swollen; *b*, *c*, one of the sides bulged out (cup form); *d*, spherical form; *e*, decolorized stroma; *f*, a thorn-apple shaped corpuscle (due to exposure); *g*, action of tannin upon a red corpuscle.

out of the corpuscle, and the colourless part or stroma remains as a faint circular outline. This simple experiment conclusively shows that **the corpuscle is composed of a membrane or external envelope with coloured fluid contents,** for the above reaction is precisely the same as would occur by osmosis with a bladder of the shape of the corpuscle filled with a strong solution of albuminous substance and placed in water (Schwann). On the other hand it is entirely inexplicable on the supposition that the corpuscle is composed of a uniform disc-shaped stroma, permeated with coloured substance, which is the view advocated by Bruecke and Rollett, and adopted by nearly all subsequent writers on the subject, for if this were the case water should swell it out uniformly; as happens if a disc of gelatine is placed in water, the whole disc imbibing the water, and become increased in size but retaining its original shape.

The same fact is illustrated by the effects of mechanical injuries. If the corpuscles are suddenly pressed they become ruptured and the hæmoglobin escapes, leaving the colourless part of the corpuscle as a mere outline. If blood is frozen the ice-crystals which form rupture the envelope, and on thawing the hæmoglobin escapes into the serum. Electric shocks passed through blood, if sufficiently strong, also rupture the delicate envelope of the corpuscles. Dilute acids act like water, but decompose the hæmoglobin into colourless proteid (globin) and hæmatin, which are both dissolved by the acid. In the case of tannic acid, the products of decomposition are usually precipitated upon the envelope in the form of a small dark red coagulum (fig. 242, *g*). Alkalies, even when very dilute, cause a complete disappearance of the red corpuscles, the membranes as well as the hæmoglobin being dissolved: the latter is converted into alkaline hæmatin. Ether or chloroform produce a similar effect when shaken up with blood, but may not completely dissolve the envelope. The blood or serum of some animals produces decolorization of the red corpuscles of others belonging to different genera. This may be due to the fact that the one is more alkaline or of less specific gravity than the other, but the actual cause has not been determined definitely. Solutions of common salt, if stronger than 0·6 per cent., produce when added to blood crenation of the red corpuscles. This is due to exosmosis, the corpuscles losing water and thereby becoming shrunken. Under like circumstances the blood-corpuscles of the frog and newt, which do not exhibit crenation, show a wrinkled appearance of the surface of the corpuscle, a phenomenon which is scarcely explicable except by assuming the presence of a membrane.

The action of ether and chloroform and that of alkalies seems to throw some

light on the nature of this membrane. For it is not easy to understand why they should produce their particular effect unless the membrane were capable of being partly or entirely dissolved by them, and this would indicate that it is largely of a fatty nature. Whether it is a pellicle of true fatty substance, or, as is more probable, a fat-like material into the composition of which the lecithin, cholesterin and proteid, which are described as composing the so-called stroma, enter, cannot here be discussed.

Various other phenomena which have been noticed in connection with the action of reagents and varying external conditions upon the red corpuscles point to the same conclusion, viz. that the external envelope of the red corpuscle is composed of a material having the physical characters of fats. A heat of 52° C. causes the coloured corpuscles to extrude globular processes and beaded filaments which may attain a relatively considerable length, and which eventually break off from the main substance of the corpuscle and form coloured globules in the fluid. A further increase of temperature to 60° C. sets free the hæmoglobin, and produces the complete disappearance of the corpuscles. Here we may suppose the fatty pellicle to become softened and eventually completely melted under the action of the increased temperature, thus permitting of the partial and eventually of the complete flowing out of its contents.

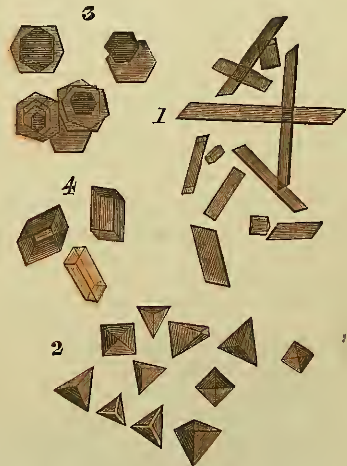

Fig. 243.—Blood-crystals, magnified.
1, from human blood; 2, from the guinea-pig; 3, squirrel; 4, hamster.

Almost any fluid which has a slight solvent action upon fats also causes an extrusion of the hæmoglobin often with disappearance of all sign of the stroma or membrane; this is the case with solutions of the bile salts. Dilute alcohol in the form of sherry wine has been noticed to produce at first the extrusion of filaments like those caused by heat (Addison); and this may be supposed also to be due to the softening or incomplete solution of a fatty pellicle. The envelopes of the corpuscles ("stromata") after complete decolorization with water or dilute acids, stain faintly, but characteristically of the presence of fatty substance, when treated with osmic acid. Finally, the presence of a fatty pellicle would of itself, as above pointed out (p. 209), furnish a sufficient explanation of the otherwise obscure phenomenon of rouleau-formation.

It has often been urged against the existence of a membranous envelope to the corpuscles that such an envelope when mechanically ruptured, as by pressure upon the corpuscles, should show signs of the gap through which the contents have escaped. This is by no means necessary, however, for in the case of a thin fatty pellicle such as that the existence of which is here assumed, the torn edges would immediately tend to come together again after rupture, and would then show no indication of the breach of continuity. A similar explanation may be given of the fact that a corpuscle may sometimes be cut into two, as when a needle is drawn sharply across a preparation of newt's blood upon a glass slide, without the coloured contents escaping from the two separated parts; in this case the pressure of the needle-point has at the same time that it severed the corpuscle brought together the opposite edges of the cut pellicle, and thus prevented the escape of the contents.

Fig. 244.—Hæmin crystals, magnified (from Preyer).

Blood in which the hæmoglobin has been dissolved out from the corpuscles has lost its opaque appearance, and has acquired a transparent laky tint; the change depends upon the fact that the colouring matter when dissolved in the serum and forming a homogeneous layer, interferes less with the transmission of light than when occurring in scattered particles.

Hæmoglobin after being thus separated from the blood-corpuscles is prone to undergo

crystallization. The crystals present various forms in different animals, but almost all (the hexagonal plates of the squirrel being alone excepted) belong to the rhombic system. From human blood and that of most mammals, the crystals are elongated prisms (fig. 243, 1), but they are tetrahedrons in the guinea-pig (2), and short rhombohedrons in the hamster (4). They are most readily obtained for microscopical examination from the blood of the rat, where they appear merely on adding a little water, and afterwards evaporating.

All hæmoglobin crystals contain a certain amount of water of crystallization. They are doubly refracting (anisotropous). The spectrum of hæmoglobin, whether in substance or in solution, may be always readily recognized by the double or single absorption bands, which are produced according as it is present in the oxidated or deoxidated condition.

Other coloured crystals, which may be obtained from blood, are the so-called "hæmin crystals" of Teichmann. They are formed when hæmoglobin is warmed with a little salt and glacial acetic acid. On cooling, the hæmin crystallizes out in minute reddish brown acicular prisms (fig. 244), the demonstration of which affords a positive proof of the presence of blood-colouring matter. They may readily be obtained from dried blood without the addition of salt, merely by warming it with glacial acetic acid.

The amount of hæmoglobin in each corpuscle, which is liable to variation, may be approximately arrived at by determining both the number of corpuscles and the amount of hæmoglobin in a given volume of blood. The amount of hæmoglobin is estimated by diluting a sample of blood with a known amount of water, and comparing the tint of the solution so obtained with that of a solution of hæmoglobin of known strength. A very convenient means of quickly obtaining an idea of the amount of hæmoglobin in a sample of blood is afforded by the "hæmoglobinometer" of Gowers, which is arranged on the above principle.

Structure of the nucleated red corpuscles of the lower vertebrata.— The large corpuscles of the frog (fig. 245) and newt differ from the mammalian

Fig. 245.—Frog's blood (Ranvier).

a, red corpuscle seen on the flat; *v*, vacuole in a corpuscle; *b*, *c*, red corpuscles in profile; *n*, pale corpuscle at rest; *m*, pale corpuscle, exhibiting amœboid movements; *p*, colourless fusiform corpuscle.

corpuscles in the possession of a nucleus. It is rather more than one-third the length of the corpuscle, but in the natural unaltered condition is visible with difficulty; this is probably owing to the fact that it possesses very nearly the same index of refraction as the rest of the corpuscle. For it may be rendered visible, even under such circumstances, by the combined action of watery vapour and carbonic acid upon the blood; a precipitate (of serum-globulin ?) is thus produced upon the nucleus, and its outline comes into view: on readmission of air the precipitate is re-dissolved, and the nucleus again becomes faint or disappears (Stricker).

The effect of most reagents is similar to that produced on human blood. Water causes both corpuscle and nucleus to swell up by imbibition, the coloured part being then extracted. A dilute solution of acetic acid in an indifferent fluid also removes the colouring matter, but the nucleus presents a markedly granular appearance (fig. 240, 3); if strong acetic acid be employed, the nucleus often acquires a reddish tint. Alkalies, on the other hand, even when very dilute, rapidly destroy both corpuscle and nucleus. Various reagents added to newt's blood cause the coloured part of the corpuscles to become partly withdrawn from the envelope, and collected around the nucleus; this is especially the case with a solution of boracic acid, the coloured matter and nucleus ("zooid" of Brücke) may subsequently be altogether extruded from the envelope or stroma of the corpuscle ("oecoid").

Dilute alcohol may bring to view one or two nucleoli within the nucleus of the amphibian red corpuscle (Ranvier, Stirling). In other respects also this structure resembles the nucleus of an ordinary cell, for it contains a network traversing its interior (fig. 246), which is, however, very close, and produces under moderate powers of the microscope a somewhat granular effect. It is doubtful whether the nucleus of the adult corpuscle can undergo division, although in the young state the division of the nucleus, followed or accompanied by that of the corpuscle, has frequently been observed.

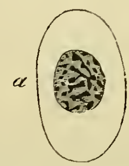

Fig. 246.—Coloured corpuscle of salamander, showing intra-nuclear network (Flemming).

COLOURLESS CORPUSCLES OF THE BLOOD.

General characters.—The white, pale, or colourless corpuscles (*leucocytes*) are few in number as compared with the red, and both on this account and because of their want of colour, they are not at first easily recognised in a microscopic preparation of blood. Their form is very various, but when the blood is first drawn they are rounded or spheroidal. Measured in this condition they are found to be about $\frac{1}{2500}$th of an inch (·01 mm. = 10 μ) in diameter. They are specifically lighter than the red corpuscles.

The white corpuscle may be taken as the type of a free animal cell. It is a minute protoplasmic structure inclosing one or more nuclei. The protoplasm, being to all appearance unaltered from its primitive condition, and unenclosed in a definite cell-wall, is capable of exhibiting in a high degree the amœboid movements

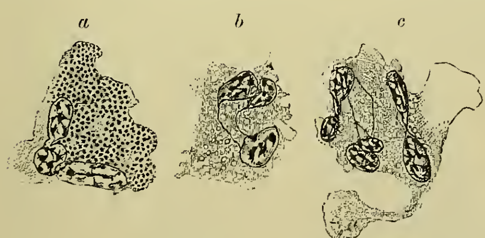

Fig. 247.—Three amœboid white corpuscles of the newt, killed by instantaneous application of steam. (E. A. S.)

a, a coarsely granular cell ; *b*, *c*, finely granular cells, with vacuolated protoplasm.

Fig. 248.—An amœboid white corpuscle of the newt. Highly magnified. (E. A. S.)

and other phenomena which depend upon the possession of contractility : these have been already sufficiently described (pp. 174 to 179). The white blood-corpuscles are apt to take into their interior minute solid particles that have been introduced into the blood (fig. 204) ; this property has served in the hands of Cohnheim and others as a means of detecting escaped white corpuscles in tissues which are wholly extravascular, such as the cornea. Some of the colourless corpuscles have in their protoplasm a number of comparatively coarse round granules (fig. 239, *g*, fig. 247, *a*) which are generally grouped together round the nucleus. These corpuscles are often distinguished from the more common paler variety (fig. 239, *p*, fig. 247, *b*, *c*) as the coarsely granular cells (eosinophile-cells of Ehrlich), but it is not known how they are different in nature, origin, or destination.

Corpuscles, coarsely granular and finely granular, are sometimes met with, which are much smaller than the ordinary pale cells, consisting chiefly of a spheroidal

nucleus with but little surrounding protoplasm. They seem to be young forms of the more protoplasmic corpuscles, and are perhaps identical with the lymphoid cells formed in lymphatic glands and similar structures.

The corpuscles often have one or more conspicuous vacuoles in their protoplasm, but these are inconstant, and may appear and disappear in the same corpuscle. Sometimes they are filled with small vacuoles so that the cell-substance assumes a frothy aspect. This is commoner in the white blood-corpuscles of the newt and other cold-blooded animals than in those of man. By means of the amœboid movement of their protoplasm, the pale corpuscles, under some circumstances, possess the power of wandering or emigrating from the blood-vessels, penetrating between the elements of their coats, and in this manner they find their way into the interstices of the tissues, and hence into the commencements of the lymphatics. Cells like these which appear to be wandering independently in the tissues, and particularly in the connective tissue, are known as *migratory* or *wander-cells*.

Besides the two forms of pale corpuscles above referred to, others have been described which differ from them in containing red-coloured granules in their protoplasm. According to A. Schmidt and Semmer, such cells are very numerous in the circulating blood, but on withdrawal of the blood from the vessels they become rapidly destroyed and disappear without leaving a trace. Schmidt looks upon them as transitional forms between the white and red corpuscles, but the evidence of their constant occurrence in normal blood is at present unsatisfactory.

The pale corpuscles possess polar particles with well-marked attraction-spheres (Flemming), and one, two, or more nuclei, which are generally obscure in the living condition, but are sometimes clearly seen when the corpuscle becomes flattened out, and may always be brought into view by reagents. The nuclei are apt to take on peculiar shapes, caused perhaps by traction exercised upon them by the movements of the surrounding protoplasm. Thus a nucleus not unfrequently becomes elongated and either irregular in outline (fig. 249) or folded on itself, so that when the ends are turned up, the appearance of two nuclei is produced, where in reality there may be but one. In fact the occurrence of several nuclei in the pale corpuscle is much more rare than is generally supposed, for it will be usually found that even when there appear to be several nuclei in a corpuscle they are united together by long strands of chromoplasm (fig. 247, *b*, *c*). In other respects they have the normal structure and appearance of cell-nuclei, containing the usual network. The division of the nucleus and of the corpuscles takes place by karyokinesis in the same way as in other animal cells. It has been observed in the lymph-cells of lymphoid tissue which afterwards become the pale corpuscles of lymph and blood, and also in some instances in corpuscles within the blood itself.

Fig. 249.—A pale corpuscle of the salamander, showing elongated irregular nucleus with intranuclear network. (Flemming.)

Action of reagents.—Water swells up and destroys the protoplasm of the white corpuscles, setting free the granules. If but little water be mixed with the drop of blood, the protoplasm may not be destroyed, but the corpuscles are swollen out (fig. 250, 1), and the granules take on an active Brownian movement. Acetic acid causes a granular precipitate in the protoplasm, the granules collecting around the nucleus, which is brought very strongly into view (fig. 250, 2, 3). A clear bleb-like swelling is also generally produced from one or more sides of the corpuscle ; but this appearance is not peculiar to acids, for it is often seen as an accompaniment of the death of the corpuscle, whether as the result of the action of reagents or from other causes. If produced by a solution of iodine, the bleb sometimes becomes coloured of a faint port-wine tint, a reaction which is generally taken as an indication of the presence of glycogen.

In the blood of the splenic vein, and also in the pulp of the spleen itself, cells have been noticed resembling pale corpuscles in their structure, but much larger, and enclosing in their

protoplasm a number of red corpuscles, or in some cases partially disintegrated portions of red corpuscles. The white corpuscles also tend to take into their protoplasm bacteria and other micro-organisms, which, according to Metschnikoff, may become destroyed within the corpuscles. They also appear to play an important part in absorption of solid and fatty particles, both from

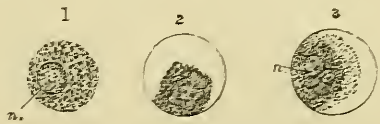

Fig. 250.—Colourless corpuscles treated with water and with acetic acid (E. A. S.).

1, first effect of the action of water upon a white blood-corpuscle; 2, 3, white corpuscles treated with dilute acetic acid; *n.* nucleus.

the intestines and in the physiological and pathological absorption of the tissues (absorption of tadpole's tail, formation of abscesses). Leucocytes which have thus "devoured" other cells or foreign substances are often termed *phagocytes*. They are often of large size, but it has not been shown that they are morphologically different from ordinary white blood-corpuscles.

Other microscopic elements in blood.—In the clear fluid which intervenes between the corpuscles, and which, in a preparation which has been made a short time, consists of serum, there can generally be detected a network of fine interlacing filaments of fibrin (fig. 251). There are also to be seen minute round colourless discoid particles in this fluid, which are usually massed together into groups, containing from a very few to an immense number of particles. They were first described under the name of *elementary particles* by Zimmermann, and attention was subsequently drawn to them by Hayem, who re-described them under the name "hæmatoblasts" as a source whence new red corpuscles are derived. Still more recently these structures have been again investigated by Bizzozero, who has termed them "blood-platelets," and has ascribed

Fig. 251.—Network of fibrin, shown after washing away the corpuscles from a preparation of blood that has been allowed to clot. (E. A. S.)

Many of the filaments radiate from small clumps of blood-tablets.

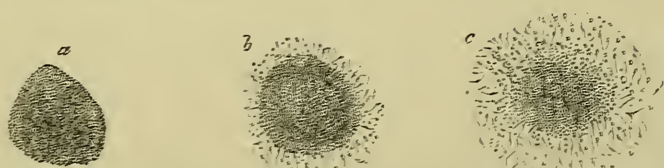

Fig. 252.—Mass of blood-platelets, showing the changes which it undergoes at its periphery when observed in salt solution on the warm stage. (Osler.)

to them special functions not only in connexion with the regeneration of the red corpuscles but also with the formation of fibrin-ferment.

It is certain that they are much more numerous in disease and especially in cachectic states of the system than in the normal condition, but they appear to be never altogether absent even in perfectly healthy blood. Löwit believes that the platelets are nothing but particles of globulin which have become precipitated from the plasma after the blood has been drawn, and others have thought that they are produced by the solution of some of the pale corpuscles, but for both these views there appears to be insufficient evidence. It was shown by Osler that they occur free within the blood-vessels (fig. 253), although they become massed together immediately the blood is drawn. The fibrin-filaments which then form, almost invariably radiate from

Fig. 253. — Blood - corpuscles and platelets within a small vein of the rat's mesentery. (Osler.)

these clumps of platelets as if they were foci for the deposition of fibrin. If the blood is mixed with salt solution (0·6 p.c.) and the preparation is maintained at a temperature of 35° to 40° C., the external platelets, together with the fibrin filaments which are adherent to them, break away from the mass and float with Brownian movement in the surrounding fluid (fig. 252).

It must be admitted that the nature and function of these elementary particles or platelets is as yet by no means clearly determined.

If blood be taken from an animal during digestion, especially of a meal containing much fatty food, the serum or plasma has a milky aspect. This is due to the presence of innumerable fine fatty particles which have been absorbed from the intestines and discharged with the chyle into the blood.

CORPUSCLES OF THE LYMPH AND CHYLE.

Lymph, when examined with the microscope, is seen to consist of a clear liquid with corpuscles floating in it. The liquid part—lymph-plasma—bears a strong resemblance in its physical and chemical constitution to the plasma of the blood. The lymph-corpuscles agree entirely in their characters with the pale corpuscles of the blood. They vary in number in lymph from different parts, being more numerous in that which has passed through the lymphatic glands than in the lymph which enters those bodies, thus indicating the lymphatic glands as an important source of these corpuscles. Many of the corpuscles found in lymph are of small size, consisting of a small amount of protoplasm and a relatively large nucleus, and thus resembling the lymphoid cells of lymphatic glands. These cells are less actively amœboid than those which are larger and contain more protoplasm. Since the lymph is poured into the blood, the lymph-corpuscles are to be looked upon as constantly furnishing a fresh supply of pale corpuscles to that fluid.

Chyle consists merely of lymph, to which are added some of the absorbed products of digestion. These are chiefly particles of fatty matter or minute oil-globules, some of which are of appreciable size, but the greater number are immeasurably small. Like the fatty globules suspended in milk, they give the chyle a similar milky aspect. These minute fatty particles were named collectively by Gulliver the "molecular base" of the chyle.

Corpuscles, like the ordinary lymph-corpuscles but with a reddish tinge, have been described in the lymph and chyle as well as in the blood, and red disks have also been noticed, but these may have got into the lymphatics accidentally through a rupture of the fine vessels.

DEVELOPMENT OF THE BLOOD-CORPUSCLES.

Origin of the white blood-corpuscles and of the corpuscles of the lymph and chyle.—The first white blood-corpuscles which are found in the embryo do not appear in the vessels so early as the coloured cells. They are in all probability amœboid mesoblastic cells, which have wandered into the blood-vessels or lymphatics. Here they may be similarly added to or they may multiply by division.

As to the origin of the lymph- and chyle-corpuscles in after life, it may be observed that the greatly increased proportion of these bodies in the vessels which issue from the lymphatic glands and organs of similar structure in various parts of the body, and the vast store of corpuscles having the same characters contained in these organs, are unmistakeable indications that they are at least a principal seat of their production. It has been shown by Flemming that a process of karyokinesis is continually going on in the lymphoid tissue, and the new cells which are thereby produced doubtless find their way into the lymphatic vessels.

Pale blood-corpuscles also, which have migrated from the vessels, may find their way into the beginning of the lymphatics. In this way the presence of corpuscles in the lymph even before it has passed through the lymphatic glands is accounted for. Lymph-corpuscles are also produced in the spleen and in the thymus gland (the latter in early life) ; and it is still believed by some authors that they may also be formed by proliferation of connective tissue corpuscles. The corpuscles of the chyle and lymph are carried into the sanguiferous system and become the pale corpuscles of the blood, but some of the latter may pass directly from the lymphatic glands, spleen, and other organs containing lymphatic or lymphoid tissue into the blood-vessels which are supplied to those organs.

Origin of the nucleated red blood-corpuscles of the embryo.—The first red blood-corpuscles are formed very early in embryonic life simultaneously with and in the interior of the first blood-vessels. They are developed in the mesoblast, in a circular area which surrounds the part of the blastoderm which is occupied by the developing body of the embryo. The area is known as the vascular area, and the first blood-vessels and blood-corpuscles are, therefore, formed outside the actual body of the embryo. The process of development is as follows :—

Those mesoblastic cells in the vascular area which are concerned with the formation of vessels (*angioblasts*) become extended into processes of varying length, which grow out from the cells in two or more directions. The cells become united with one another, either directly or by the junction of their processes, so that an

Fig. 254.—Part of the network in developing blood-vessels in the vascular area of the guinea-pig. (E. A. S.)

bl, blood-corpuscles becoming free in an enlarged and hollowed out part of the network. The smaller figure on the left represents *a* of the larger figure, more highly magnified ; *d*, a nucleus undergoing division.

irregular network of protoplasmic nucleated corpuscles is thus formed (fig. 254). Meanwhile the nuclei become multiplied, and whilst the greater number remain grouped together in the original cell-bodies or nodes of the network, some are seen in the uniting cords. The nuclei which remain in the nodes accumulate, each one around itself, a small amount of cell-protoplasm. The corpuscles thus formed (*bl*) acquire a reddish colour, and the protoplasmic network in which they lie becomes vacuolated and hollowed out into a system of branched canals enclosing fluid, in which the nucleated coloured corpuscles float. The intercommunicating canals gradually become enlarged so as to admit of the passage of the corpuscles. The protoplasm which forms the wall of these first vessels becomes differentiated around the nuclei which have remained embedded in it, so as to give rise to the flat cells which compose the blood-capillaries.

As soon as the heart is developed, or even before this happens, the blood begins

to move within the vessels of the vascular area. And when the action of the heart commences, the blood is driven also through vessels which are formed, probably in a manner similar to that above described, in the mesoblast of the body of the embryo.

These first formed red blood-corpuscles are nucleated cells resembling the pale corpuscles except in their colour and in the clearness of their protoplasm, and, like the white corpuscles, they are capable of amœboid movement, and of undergoing multiplication by division. It is uncertain whether, as stated by Kölliker and others, any of the primary red blood-corpuscles are produced by direct transformation of individual cells of the mesoblast, but (whether by accession of some of these last, by division, or by a continuance of the original mode of formation), the numbers increase considerably, and they are soon accompanied by colourless corpuscles. These appear to be formed in great number in the embryonic liver as soon as this is developed, as well as in the lymphatic glands, spleen and thymus gland. It has been supposed that the colourless corpuscles formed in these organs acquire colour, and are converted into nucleated red corpuscles, but there is no direct evidence in favour of this view.

The primary nucleated red corpuscles are at length succeeded by smaller disk-shaped red corpuscles without nuclei, having all the characters of the blood-disks of the adult. This substitution proceeds gradually, until, long before the end of intra-uterine life, the *nucleated* red corpuscles have almost entirely vanished from the blood. According to Neumann, some are still to be met with even in the new-born child. It is probable that they are converted into non-nucleated disks, but it is not known how the transformation occurs. Probably the process is the same as that which takes place in the case of the nucleated red corpuscles of the red marrow of the adult, which are indeed in all likelihood the direct descendants of the embryonic nucleated blood-corpuscles.

Origin of the red blood-disks.—1. Intracellular origin. The disk-shaped red corpuscles are produced in the interior of angioblastic connective tissue cells in the following manner :—

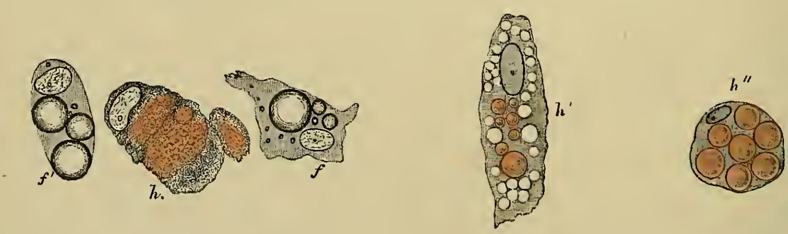

Fig. 255.—Development of red corpuscles in connective tissue cells (angioblasts). From the subcutaneous tissue of the new-born rat. (E. A. S.)

h, a cell containing hæmoglobin in a diffused form in the protoplasm ; *h′*, one containing coloured globules of varying size, and vacuoles ; *h″*, a cell filled with coloured globules of nearly uniform size ; *f*, *f′*, developing fat cells.

A part of the protoplasm of the cell acquires a reddish tinge (fig. 255, *h*), and after a time the coloured substance becomes condensed in the form of globules (*h′*) within the cells, varying in size from a minute speck to a spheroid of the diameter of a blood-corpuscle, or even larger ; but gradually the size becomes more uniform (fig. 255, *h″*). Some parts of the embryonic connective tissue, especially where a vascular tissue, such as the fat, is about to be developed, are completely studded with cells like these, occupied by a number of coloured spheroids and forming nests of blood-corpuscles or minute "blood-islands." After a time the cells become elongated and pointed at their ends, and processes grow out to join prolongations of

neighbouring blood-vessels or of similar cells. At the same time vacuoles form within them (fig. 255, h'), and becoming enlarged coalesce to form a cavity filled with fluid, in which the reddish globules, which are now becoming disk-shaped, float (fig. 256). Finally the cavity extends through the cell-processes into those of neighbouring cells, and a vascular network is produced, and this becomes eventually united with pre-existing blood-vessels, so that the blood-corpuscles which have been formed within the cells in the manner described, get into the general circulation (see Development of Blood-vessels).

This "intracellular" mode of development of red blood-corpuscles ceases in most animals before birth, although in those which, like the rat, are born very immature, it may be continued for a few days after birth. Subsequently, although new vessels are formed in the same way, blood-corpuscles are not produced within them, and it becomes necessary to seek for some other source of origin of the red blood-discs, both during the remainder of the period of growth, and also during adult life, for it is certain that the blood-corpuscles are not exempted from the continual expenditure and fresh supply which affect all the other tissues of the body.

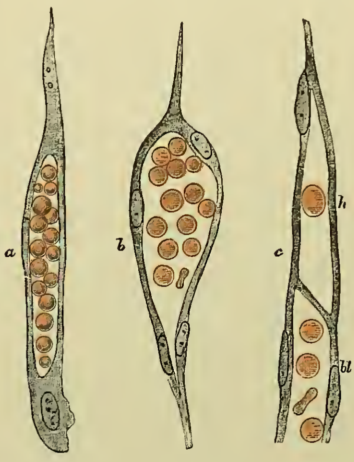

Fig. 256.—Further development of blood-corpuscles within connective tissue cells, and transformation of the latter into capillary blood-vessels (E. A. S.)

a, an elongated cell with a cavity in its protoplasm occupied by fluid and by blood-corpuscles which are still globular; *b*, a hollow cell the nucleus of which has multiplied. The new nuclei are arranged around the wall of the cavity, the corpuscles in which have now become discoid; *c*, shows the mode of union of an angioblast, which in this instance contains only one corpuscle, with the prolongation (*bl*) of a previously existing vessel. *a*, and *c*, from the new-born rat; *b*, from a fœtal sheep.

2. In the marrow of bones.—In the red marrow which fills the internal cavities of many bones, and particularly the ribs, corpuscles have been observed which appear to justify the inference that red blood-corpuscles are here becoming developed. These corpuscles, which have been termed *erythroblasts*, were long ago described by Neumann, and by Bizzozero, and have since been noticed also by many other observers, by most of whom they are stated to be formed from the leucocytic marrow-cells. The accounts are, however, somewhat different; for, according to some, the *nucleus* of the marrow-cell becomes coloured, and with a small amount of protoplasm persists as the red disc, while others describe the *protoplasm* as becoming transformed into the red corpuscle whilst the nucleus disappears.

According to the account given by Bizzozero, the erythroblasts are not developed from the leucocytic marrow cells, nor from the white corpuscles of the blood, but are corpuscles *sui generis*, which multiply by karykinesis, and become gradually transformed, in the mammalia with disappearance of the nucleus, into the red blood-disks. My own observations are entirely in accordance with these statements. The coloured cells that I have noticed have almost always been distinctly smaller than the ordinary marrow-cells, often of irregular forms, and sometimes

Fig. 257.—Coloured nucleated cells from the red marrow of the guinea-pig (E. A. S.)

appear to be undergoing division (fig. 257). They are amœboid cells, the protoplasm of which is coloured by hæmoglobin, and they closely resemble, in fact, the nucleated red blood-corpuscles of the embryo. It appears therefore probable that the cells in question are descendants of the embryonic red blood-corpuscles, and that they are transformed into the ordinary blood-discs by the gradual atrophy and disappearance of the nucleus and the moulding of the coloured cell-substance into the shape of the biconcave red corpuscles. Appearances such as are exhibited by some of the corpuscles which are delineated in fig. 257, certainly indicate atrophy of the nucleus.[1] The amœboid movements of which these corpuscles are capable may assist them to pass into the blood-capillaries, the walls of which are, in mammals, less distinct and continuous than in other parts, with the single exception of the spleen. But it would appear from the observations of Bizzozero and Torre that in birds the capillary walls are complete, and that all the erythroblasts are intravascular, *i.e.*, are found within the venous capillaries and not in the tissue of the marrow. These venous capillaries are relatively large, and the blood-stream in them must be exceedingly slow. The fully developed red corpuscles lie in the axis of the vessel, the erythroblasts and leucocytes towards the periphery.

These statements have been confirmed in the main by Denys, who has also subjected the marrow in birds to a careful examination. Denys states, however, that the coloured erythroblasts are derived from colourless erythroblasts lying next to the capillary wall, and that while this transformation into red corpuscles is going on within the vessels, the marrow cells outside the vessels are multiplying and forming white blood corpuscles.

3. **Origin from white corpuscles.**—The view which long obtained most prevalence, is that the red discs are developed from the white corpuscles. There are, however, no recorded observations of recent date which show conclusively that the red corpuscles are thus developed in the circulating blood, although some observers are of opinion that such transformation may occur in the marrow.

4. **In the spleen.**—It has long been believed that the formation of red blood-corpuscles is carried on in the spleen-pulp, but this view has been in many quarters supplanted by the contrary one that a destruction of red corpuscles rather than a new formation may there take place, in support of which many facts were brought forward by Kölliker. The former view has, however, been again brought into prominence by Bizzozero, who describes in the spleen-pulp after severe loss of blood, nucleated red corpuscles like those in the marrow, and further finds that there are more red as well as white corpuscles in the blood of the splenic vein than in that of the corresponding artery. These statements only apply, however, to certain animals.

5. **From the elementary particles or blood-platelets.**—Hayem described these as the precursors of the red blood-corpuscles in mammals. To them he applied the name "hæmatoblasts," and he maintains that they acquire colour, and by a gradual increase in size become directly transformed into red corpuscles. In support of this view he points out that red corpuscles which are much smaller than the ordinary ones are to be almost always met with in blood, and that these smaller forms are especially numerous in cases where there has been previously a considerable loss of blood, and in which, therefore, it may well be supposed that a new formation of red corpuscles is proceeding; and further, that they present every transition between the blood-tablets and the red discs.[2] In the frog Hayem describes as hæmatoblasts, spindle-shaped cells something like the white corpuscles, but of more delicate appearance (like the corpuscle marked *p* in fig. 245). These become, according to him, converted directly into red corpuscles, after undergoing an increase of size and a change of shape, in addition to the accession of colouring matter. They had been long previously noticed by Recklinghausen, and regarded as transition forms between the white and red corpuscles.

Morphology of the red corpuscles.—It is obvious from the study of the structure of the mammalian red blood-disks that they are not morphologically to be regarded as cells. For they lack a most important morphological constituent of the cell, viz., the nucleus, nor do they exhibit any other sign of cell-structure.

[1] According to Howell the partially atrophied nucleus becomes extruded, and then dissolved.

[2] A similar account of the development of the red discs was given by Zimmermann; but many of the transitional forms which he described were red corpuscles which had become decolorised. The same may probably be said regarding the "invisible corpuscles" of Norris ("Physiology and Pathology of the Blood," 1882).

Chemically also, as has been shown by Halliburton and Friend, the red corpuscles lack substances, such as cell-albumin and nucleo-albumin, which are characteristic of typical animal cells. They contain, however, a small amount of cell-globulin, and this appears to be their only proteid. Further, although originally formed from and within protoplasm (see above, Intracellular development, and Development in marrow), they have lost all amœboid properties—in fact, as the study of their formation within the angioblasts shows, the protoplasm from which they are formed becomes transformed into little but a solution of hæmoglobin, which as their development proceeds, becomes confined by a delicate pellicle of "stroma substance." This may itself be a deposit formed around the hæmoglobin-globules by the cell-protoplasm, or may be a modified remainder of that protoplasm which is left around the globule.

On the other hand, the nucleated red corpuscle of oviparous vertebrates, although its general structure and mode of development show it to be morphologically a cell, yet has in the adult none of the functional characteristics of cells. Nor so far as we know is it in the adult condition capable of undergoing division and multiplication, although the nucleus retains the structure and chemical composition which is typical of cell-nuclei. The cell-body, on the other hand, has both histologically and chemically lost the properties of cell-protoplasm, and as in the case of the mammalian corpuscle is wholly transformed into a homogeneous mass or solution of hæmoglobin with a delicate enclosing pellicle. Some authors have, it is true, described a reticular structure within these corpuscles, but there is little doubt that such reticulum has been artificially produced by the reagents used to fix the corpuscles. These nucleated corpuscles of ovipara differ from the nucleated corpuscles of the mammalian embryo, for the latter are true functional cells, capable of division, and exhibiting amœboid phenomena, and in short differing from a typical animal cell, such as the white corpuscle, only in the presence of hæmoglobin in their protoplasm. The nucleated coloured cells of the marrow are in all respects similar to them.

Historical.—The development of blood-corpuscles in isolated patches in the vascular area of the chick was first recognised by Pander, who termed the patches "blood-islands." Remak, and after him, His and Kölliker, described the first vessels in the vascular area of the chick as originating in the form of a solid cord of mesoblastic cells, arranged so as to form a network; the peripheral cells of the vascular cords becoming flattened and forming the epithelium of the vessels, whilst the centrally placed cells become directly converted into blood-corpuscles, acquiring colour first of all at certain points—the blood-islands of Pander—and fluid accumulating between them to form the liquor sanguinis. His stated, moreover, that the blood-vessels within the body of the embryo originate as ingrowths from these vessels of the vascular area.[1] Stricker was the first to describe the formation of blood-vessels by the hollowing out of connective tissue-cells, and Afanasieff and Klein proved that the blood-islands of Pander were cells of the mesoblast, in the interior of which blood-corpuscles had made their appearance, and that the containing cells became the first blood-vessels. Klein's account was confirmed, and in some particulars modified, by Balfour. The account above given of the formation of vessels and blood-corpuscles in the vascular area of mammals is derived from observations upon the embryo of the guinea-pig. The production of red blood-disks in the interior of certain cells of the connective tissue was first noticed by me in the subcutaneous connective tissue of the new-born rat, and subsequently in the embryos of a number of different animals, and these observations were confirmed by Ranvier—who terms the connective tissue-cells concerned in the process "vasoformative cells"—as well as by Leboucq and others. The discovery of the important fact that in the adult condition the main if not the only seat of formation of red blood-corpuscles is the red marrow of the bones, is due to the researches of Neumann, which were first published in 1868.

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[1] Vide Embryology, p. 25.

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CONNECTIVE TISSUE PROPER.

Areolar tissue.—If we make a cut through the skin and proceed to raise it from the subjacent parts, we observe that it is loosely connected to them by a soft filamentous substance of considerable tenacity and elasticity, and having, when free from fat, a white fleecy aspect; this is the substance known as *areolar tissue.* In like manner the areolar tissue is found underneath the serous and mucous membranes which are spread over various internal surfaces, and serves to attach these membranes to the parts which they line or invest; and as under the skin it is named "subcutaneous," so in the last-mentioned situations it is called "subserous" and "submucous" areolar tissue. But on proceeding further we find this substance lying between the muscles, the blood-vessels, and other deep-seated parts, occupying, in short, the intervals between the different organs of the body where they are not otherwise insulated, and thence named "intermediate;" very generally, also, it becomes more consistent and membranous immediately around these organs, and under the name of the "investing" areolar tissue, affords each of them a special sheath. It thus forms inclosing sheaths for the muscles, the nerves, the blood-vessels, and other parts. Whilst the areolar tissue might thus be said in some sense both to connect and to insulate entire organs, it also performs the same office in regard to the finer parts of which these organs are made up; for this end it enters between the fibres of the muscles, uniting them into bundles; it connects the several membranous layers of the hollow viscera, and binds together the lobes and lobules of compound glands; it also accompanies the vessels and nerves within these organs, following their branches nearly to their finest divisions, and affording them support and protection. This portion of the areolar tissue has been named the "penetrating," "constituent," or "parenchymal."

It thus appears that the areolar is one of the most general and most extensively distributed of the tissues. It is, moreover, continuous throughout the body, and from one region it may be traced without interruption into any other, however distant; a fact not without interest in practical medicine, seeing that in this way dropsical waters, air, blood, and urine, effused into the areolar tissues, and even the matter of suppuration, when not confined in an abscess, may spread far from the spot where they were first introduced or deposited.

On stretching out a portion of areolar tissue by drawing gently asunder the parts between which it lies, it presents an appearance to the naked eye of a multitude of fine, soft, and somewhat elastic threads, quite transparent and colourless, like spun glass; these are intermixed with fine transparent films, or delicate membranous laminæ, and both threads and laminæ cross one another irregularly and in all imaginable directions, leaving open interstices or areolæ between them. These meshes are, of course, more apparent when the tissue is thus stretched out; it is plain also that they are not closed cells, as the term "cellular tissue" which was formerly used to denote the areolar tissue, might seem to imply, but merely interspaces, which open freely into one another: many of them are occupied by the fat, which, however, does not lie loose in the areolar spaces, but is enclosed in its own vesicles. A small quantity of colourless transparent fluid of the nature of lymph is also present in the areolar tissue, but, in health, not more than is sufficient to moisten it.

On comparing the areolar tissue of different parts, it is observed in some to be more loose and open in texture, in others more dense and close, according as free movement or firm connection between parts is to be provided for.

Fibrous tissue.—When the fine bundles of connective tissue are disposed for the most part in one or two directions, instead of interlacing in every direction as

in the areolar tissue, they confer a distinctly fibrous aspect to the parts which they compose, accompanied by the acquisition of certain properties, which are mainly due to the parallel disposition of the elements of the tissue, and to the preponderance of the white fibres over the elastic (see below). This *fibrous tissue* is met with in the form of ligaments, connecting the bones together at the joints ; it also forms the tendons of muscles, into which their fleshy fibres are inserted, and which serve to attach these fibres to the bones. In its investing and protecting character it assumes the membranous form, and constitutes a class of membranes termed "fibrous." Examples of these are seen in the periosteum and perichondrium which cover the bones and cartilages, in the dura mater which lines the skull and protects the brain, and the fibrous layer which strengthens the pericardium, also in the albugineous coat of the testicle, and the sclerotic coat of the eye, which enclose the tender internal parts of these organs. Fibrous membranes, named "aponeuroses" or "fasciæ," are also employed to envelop and bind down the muscles of different regions, of which the great fascia inclosing the muscles of the thigh and leg is a well-known example. The tendons of muscles, too, may assume the expanded form of aponeuroses, as those of the broad muscles of the abdomen, which form strong fibrous layers in the walls of that cavity and add to their strength. It thus appears that the fibrous tissue presents itself under two principal forms, the *fascicular* and the *membranous.*

The fibrous tissue is white, with a shining, silvery, or pearly aspect. It is exceedingly strong and tough, yet perfectly pliant ; but it is almost devoid of extensibility. By these qualities it is admirably suited to the purposes to which it is applied in the animal frame. By its inextensible character it maintains in apposition the parts which it connects against any severing force short of that sufficient to cause actual rupture, and this is resisted by its great strength, whilst its flexibility permits of easy motion. Accordingly the ligaments and tendons do not sensibly yield to extension in the strongest muscular efforts ; and though they sometimes snap asunder, it is well known that bones will break more readily than tendons of equal thickness, and the fibrous membranes are proportionally strong and alike inextensible.

Elastic tissue.—In other situations in the body a tissue is found which, while allowing a considerable amount of extension, will readily return to its original condition when the extending force is relaxed. This is provided for by the preponderance of elastic fibres in the connective tissue, and these in the most typical examples of the tissue, such as the ligamentum nuchæ of quadrupeds and the ligamenta subflava of the human spine, give it a yellowish colour. The tissue is extensible and elastic in the highest degree, but is not so strong as ordinary fibrous ligament, and it breaks across the direction of its fibres when forcibly stretched.

Examples of the texture on a large scale are seen in the horse, ox, elephant, and other large quadrupeds, in which it forms the great elastic ligament, called *ligamentum nuchæ,* that extends from the spines of the vertebræ to the occiput and aids in sustaining the head ; in the same animals it also forms an elastic subcutaneous fascia, which is spread over the muscles of the abdomen and assists in supporting the contents of that cavity. In the human body it is met with chiefly in the following situations, viz. :—

1. Forming the *ligamenta subflava,* which extend between the arches of adjacent vertebræ ; these ligaments, while they permit the bones to be drawn apart in flexion of the body, aid in restoring and maintaining their habitual approximation in the erect posture—so far, therefore, relieving the constant effort of the erector muscles. There is, moreover, an obvious advantage in having an elastic band in this situation, instead of an ordinary ligament, which would be thrown into folds when the bones are approximated. 2. Constituting the chief part of the stylohyoid, thyrohyoid, and cricothyroid ligaments, and those named the vocal cords. Also

extending, in form of longitudinal bands, underneath the mucous membrane of the windpipe and its ramifications. 3. Entering, along with other textures, into the formation of the coats of the blood-vessels, especially the arteries, and conferring elasticity on these tubes.

MICROSCOPIC STRUCTURE OF CONNECTIVE TISSUE.

The three kinds of connective tissue, the obvious characters and arrangement of which have just been described, agree closely with one another in elementary structure. They are all composed of a matrix or ground-substance, in which cells are imbedded, and in this ground-substance and between the cells are fibres of two kinds, the white and elastic. It is the different arrangement of the cells and fibres, as well as the relative proportion of one kind of fibre to the other, that determines the different characters of the varieties of connective tissue above enumerated.

Ground-substance of connective tissue.—The ground-substance, matrix, or intercellular substance of the connective tissue is composed of a soft homogeneous material which occupies the tissue between the cells and cell-groups, and in which, as above stated, the fibrous elements of the tissue are found, it may be in so great a quantity as altogether to obscure the ground-substance in which they lie. It serves thus to unite the fibres, at least the white fibres, into the bundles which they form, penetrating between the individual fibrils of a bundle, and enveloping the latter with a homogeneous sheath often of great tenuity.

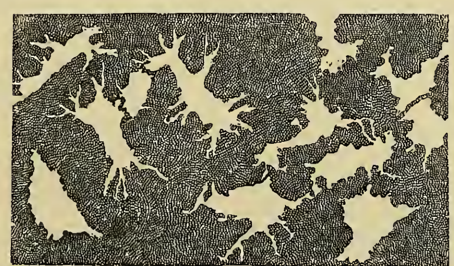


Fig. 258.—Cell-spaces of subcutaneous connective tissue, the ground substance having been stained deeply by nitrate of silver. (E. A. S.) 340 diameters.

The ground-substance of connective tissue appears to contain mucin. It is precipitated and rendered cloudy by acetic acid. It becomes stained brown when treated with nitrate of silver and afterwards exposed to the light, in this respect resembling the intercellular substance of an epithelium. The cells of the tissue lie imbedded in it, either in shallow pits on the surface, or in spaces—*cell-spaces*—entirely enclosed by the ground-substance, the spaces being for the most part rather larger than the contained cells, with which, however, they correspond on the whole in shape. These cell-spaces (*Saft-kanälchen* of Recklinghausen, *lymphatic canaliculi* of Klein and Burdon-Sanderson) are brought into view when the tissue is stained with nitrate of silver, for they then look white upon the brown ground (fig. 258).

White Fibres.—When examined under the microscope both the areolar and fibrous tissues appear to be principally made up of exceedingly fine, transparent, and homogeneous filaments, from about $\frac{1}{50000}$ to $\frac{1}{25000}$th of an inch in thickness, or even less (fig. 259). These are seldom single, being mostly united by means of a small and usually imperceptible quantity of the ground-substance into bundles and filamentous laminæ of various sizes, which to the naked eye appear as simple threads and films. Though the bundles may intersect in every direction, the filaments of the same bundle run nearly parallel to each other, and no one filament is ever seen to divide into branches or to unite with another. The associated filaments take an alternate bending or waving course as they proceed along the bundle, but still maintain their general parallelism. This wavy aspect, which is very characteristic of these filaments, disappears on stretching the bundle, but returns again when it is relaxed.

The filaments just described, though transparent when seen with transmitted light under the microscope, appear white when collected in considerable quantity and seen with reflected light ; they are doubly refracting and, therefore, appear bright when viewed between crossed Nichol's prisms. Acetic acid causes them to swell up and become indistinct. When the tissue is boiled in water the white fibres are resolved into gelatine. They are not digested by trypsin.

Fig. 259.—Filaments of areolar tissue, in larger and smaller bundles, as seen under a magnifying power of 400 diameters. (Sharpey.)

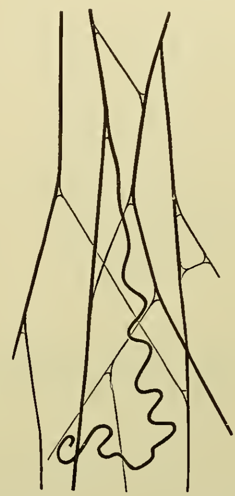


Fig. 260.—Elastic fibres of connective tissue.

(From the subcutaneous tissue of the rabbit.)

Elastic Fibres.—Occurring both in the areolar and fibrous tissue, and composing the greater part of the so-called elastic connective tissue, fibres of a different nature from those just considered are found—these are the elastic fibres. When collected in considerable quantity they have, as before stated, a yellowish colour, but when seen singly their yellow colour does not appear ; they can, however, always be recognised by the following characters. When viewed under a tolerably high magnifying power, they appear homogeneous and highly refracting, with a remarkably well-defined outline. They may run nearly straight, but may follow a somewhat bending course, with bold and wide curves, unlike the small undulations of the white connective filaments. As they proceed they divide into branches, and join or anastomose together in a reticular manner (figs. 260, 262). In some parts the elastic networks are composed of fine fibres with wide meshes ; in other parts the elastic fibres are larger and broader and the intervening spaces narrower, so that the tissue may even have a lamellar character and present the appearance of a homogeneous membrane, which may be either entire, or with gaps or perforations at short intervals, in which case it constitutes the fenestrated membrane of Henle, found in the coats of the blood-vessels. A character which elastic fibres exhibit in many specimens, is a tendency to curl up at their broken ends (figs. 260, 261) ; and these ends are not pointed, but abruptly broken across. Their size is very various ; the largest in man are nearly $\frac{1}{4000}$th of an inch in diameter, the smallest perhaps not more than $\frac{1}{24000}$th. In some situations the larger sized fibres prevail ; this is the case with the ligamenta subflava, where their general diameter is about $\frac{1}{7500}$th of an inch ; in other instances, as in the vocal cords and in many parts of the areolar

tissue, the elastic fibres are exceedingly fine. In some animals elastic fibres are met with $\frac{1}{1500}$th of an inch in thickness. In shape they are not cylindrical but angular, as is well seen in transverse section (fig. 266).

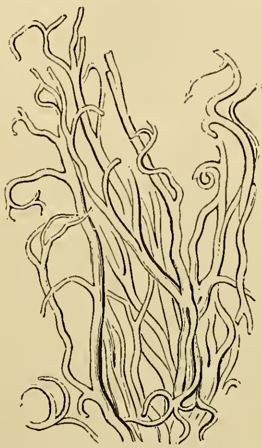


Fig. 261.—Elastic fibres from the ligamenta subflava; magnified about 200 diameters. (Sharpey.)

In certain portions of the areolar tissue, as for instance in that which lies under the serous and mucous membranes of particular regions, the yellow or elastic fibres are abundant and large, so that they cannot well be overlooked; but in other parts and in the fibrous tissue, they are few in number, and small, and are then in a great measure hidden by the white filaments; in such cases, however, they can generally be rendered conspicuous under the microscope by means of acetic acid, which causes the white filaments to swell up and become indistinct, whilst the elastic fibres not being affected by that re-agent, come then more clearly into view.

Watery solutions of magenta and many other aniline dyes stain elastic fibres very intensely. Elastic fibres do not yield gelatine on boiling. They are composed of a substance named *elastin*, which is enclosed in a membrane or sheath (Schwalbe). This membrane resists the action of digestive ferments, and also that of acids and alkalies, which break the elastin up into globules and eventually dissolve it (Pfeuffer, Mall). According to Mall this membrane is chemically similar to the reticulum of retiform tissue.

Many observers have described transverse striation in elastic fibres (see fig. 265), especially in those that have been long macerated. It is not improbable that appearances of transverse

Fig. 262.—Subcutaneous areolar tissue from a young rabbit. Highly magnified. (E. A. S.)

The figure shows the appearance of the tissue examined perfectly fresh in a preparation made by the demi-dessication method and moistened only with lymph.

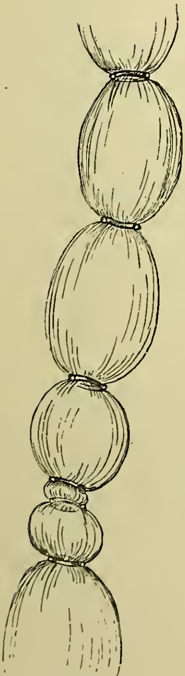
The white fibres are in wavy bundles, the elastic fibres form an open network. *p*, *p*, vacuolated cells (plasma cells); *g*, granular cell; *c*,*c*, branching lamellar cells; *c'*, a flattened cell of which only the nucleus and some scattered granules are visible; *f*, fibrillated cell.

Drawn under Zeiss' 2 mm. apochromatic homogeneous-immersion objective, and No. 8 compensating eyepiece.

striation, and also the tendency which the elastic fibres show to break across (seldom or never splitting longitudinally), are indications of the original formation of the fibres as rows of isolated particles, which subsequently become fused together.

In **areolar tissue** the bundles of white fibres intercross in all directions (fig. 262), and exhibit every degree of curvature. The bundles are very variable in size, the number of filaments in a bundle presenting a corresponding variation ; and the laxity or density of the tissue depends chiefly upon the size of the bundles and the closeness with which they are packed.

The elastic fibres of areolar tissue run in the ground-substance between the white bundles, but when the latter are large and occupy almost the whole of the tissue the elastic fibres often appear to lie upon the surfaces of the bundles, and we even see here and there what appears to be an elastic fibre winding round one of these bundles, and encircling it with several spiral turns. When acetic acid is applied, the fasciculus swells out between the constricting turns of the winding fibre, and presents a highly characteristic appearance (fig. 263). This remarkable disposition of the elastic fibres, which was pointed out by Henle, is not uncommon



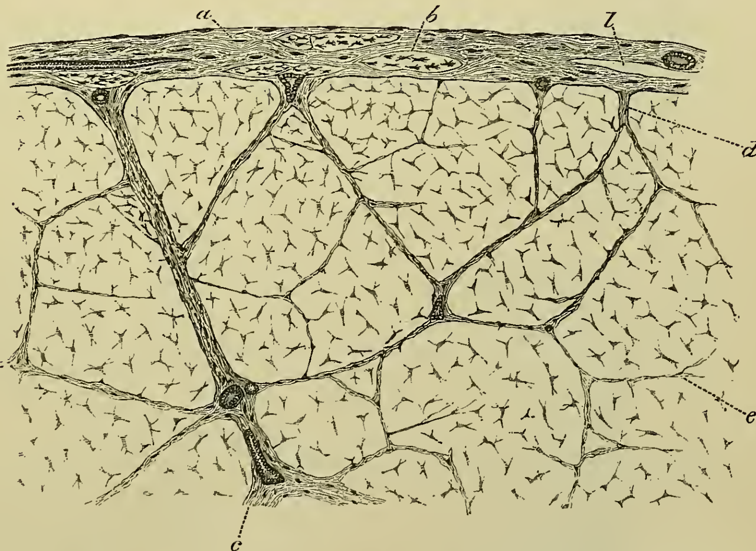


Fig. 263.—Bundle of white fibres of connective tissue swollen by acetic acid. (Toldt.) From the subarachnoid tissue at the base of the brain.

Fig. 264.—Part of a moderately large tendon in transverse section. (E. A. S.)

a, areolar sheath of the tendon, with the fibres for the most part running transversely, but with two or three longitudinal bundles, *b* ; *l*, lymphatic cleft in the sheath ; immediately over it a blood-vessel is seen cut across and on the other side of the figure a small artery is shown cut longitudinally ; *c*, large septum of areolar tissue ; *d*, smaller septum ; *e*, still smaller septum. The irregularly stellate bodies are the tendon cells in section.

in certain parts of the areolar tissue ; it may be always seen in that which accompanies the arteries at the base of the brain. It must be observed, however, that the encircling fibre sometimes forms not a continuous spiral, but several separate rings. In such a case the appearance may be explained on the supposition that the bundles in question are naturally invested with a delicate sheath, which, like the elastic tissue, resists acetic acid, but, on the swelling up of the bundle under

the operation of that agent, is rent into shreds or segments, mostly annular or spiral, which cause the constrictions. In other cases the union of branches of the cells around a bundle may be the cause of the appearance.

The areolæ, or interstices of the areolar tissue, are intercommunicating cleft-like spaces between the bundles and laminæ. They are not present in the immature tissue, in which the ground-substance is continuous throughout, but as the matrix becomes fibrillar the areolæ are formed, probably by the liquefaction of ground-substance.

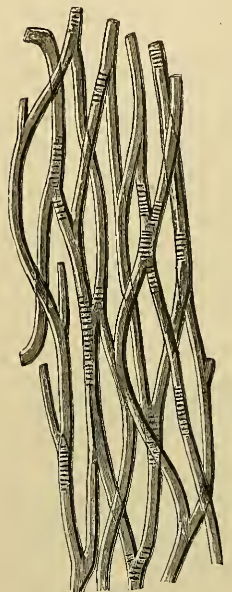


Fig. 265.—Elastic fibres from the ligamentum nuchæ of the ox, showing transverse markings on the fibres; highly magnified. (E. A. S.)

In **fibrous tissue** the bundles of white filaments run parallel, cohering very intimately. They either run all in one direction as in long tendons, or intersect each other in different planes as in some aponeuroses, or they take various directions and decussate irregularly with each other as in the dura mater. And when they run parallel to each other, as in tendon, they do not keep separate throughout their length, but send off slips to join neighbouring bundles and receive the like in turn; so that successive cross-sections of a tendon or ligament present different figures of the sectional areas of the bundles. A sheath of dense areolar tissue covers the tendons and ligaments on the outside (fig. 264, *a*), and a variable amount of the same tissue (*d*, *e*) lies between the fasciculi into which the smaller bundles are grouped, separating them from one another, and also occurring, in greater amount, between the largest fasciculi (*c*). It is in these areolar tissue septa that the blood-vessels and lymphatics of a tendon or ligament run.

The surface of a tendon or of any other part consisting of this texture, appears marked across the direction of the fasciculi with alternate light and dark streaks which give it a peculiar aspect, not unlike that of a watered ribbon. This appearance is owing to the wavy course of the filaments, for when the light falls on them their bendings naturally give rise to alternate lights and shadows.

The fibrous and areolar tissues thus agreeing in their ultimate structure, it is not to be wondered at that sometimes the limits between the two should be ill-defined, and that the one should pass by inconspicuous gradations into the other. Instances of such a transition may be seen in many of the fasciæ: these at certain parts consist of dense areolar tissue, but on being traced farther are seen gradually to become fibrous; and fasciæ, which in one body are areolar in character, may be decidedly fibrous in another.

Fig. 266.—Cross-section of elastic fibres from the ligamentum nuchæ of the ox (drawn by T. P. Gostling.)

In the **elastic tissue**, there is a great proportionate development of the elastic fibres, the white bundles being relatively few and indistinct, but considerable variation is met with in the proportion of the two kinds of elements. The white bundles are, for the most part, disposed irregularly and course in different directions, as in areolar tissue; but, in some elastic ligaments, there are bundles of white fibres, which run as in an ordinary ligament parallel with one another, and from end to end of the structure. The elastic fibres in an elastic liga-

ment, are collected into smaller and larger groups or bundles (fig. 266), which are separated from one another by septa of the white tissue, but the latter also penetrates between the individual elastic fibres of the group.

The cells or corpuscles of connective tissue.—Three kinds of cells may be distinguished in connective tissue, and these may provisionally be termed the *flattened or lamellar*, the *granular*, and the *vacuolated* or *plasma-cells*. They are all imbedded in the ground-substance, occupying the cell-spaces previously mentioned.

The *flattened or lamellar cells* (fig. 262, *c*, *c* and fig. 267), are often applied to the surfaces of the bundles of white fibres. Where three or more bundles come into

Fig. 267.—Two connective tissue corpuscles from the subcutaneous connective tissue; highly magnified. (E. A. S.)

The dark streak below *l*, in the right hand corpuscle, is a lamella which happens to be projecting towards the observer and is seen in optical section.

apposition, the cells may extend between the several bundles, and they then consist of not one lamella, but of two, three, or more which fit in between the bundles, the body of the cell occupying the larger interstice. This is most marked in fibrous tissue, but is also seen in dense areolar tissue. The cells in some parts are united

Fig. 268.—Ramified connective tissue corpuscles. (E. A. S.) 250 diameters.
(From a preparation stained with chloride of gold.)

Fig. 269.—Epithelioid and ramified cell-spaces of connective tissue. (E. A. S.) 340 diameters.
(From a preparation stained with nitrate of silver.)
The nuclei of the cells are indicated.

by their edges into patches, after the manner of an epithelium ; in other cases, a union takes place by means of branching processes, so that the cells form a kind of network throughout the ground-substance, and a corresponding network is of course formed by the spaces in which the cells lie (figs. 268, 269). These flattened connective tissue corpuscles are composed of clear cell-substance, with but a few

minute granules scattered through it; they have a large oval nucleus with a fine intra-nuclear network and nucleoli.

In many membranous forms of connective tissue, the flattened cells form an epithelial-like covering to the surfaces of the membrane or membranes (fig. 270), and may even complete the latter by bridging over any gaps existing between the bundles of fibres forming the membrane. Such epithelioid tracts may be of considerable extent. It is often observable, that the cells at the margin of the patch have processes at their free border, which are connected with the ordinary scattered cells of the tissue (see fig. 269).

Granular cells.—Besides these flattened cells with fine granules, other corpuscles are met with in the connective tissue, which are more decidedly granular (fig. 262, *g*), having actual distinct, somewhat coarse, granules in their protoplasm. Although they were classed along with the vacuolated cells, next to be described, by

Fig. 270.—Epithelioid cells of connective tissue. From the surface of an aponeurosis treated with nitrate of silver. Highly magnified. (E. A. S.)

Waldeyer, under the name of plasma-cells, they are perfectly distinct elements, and it will be better therefore to reserve the name "plasma-cells" for the vacuolated corpuscles, and to employ the name of granular cells for these, which are filled with obvious granules. The granular cells are especially abundant near the blood-vessels, and they also occur in large number in areolar tissue in which fat is to be deposited. The granules are of an albuminous nature; they stain deeply with eosin[1] and with many aniline dyes. These cells vary much in size and shape; many are spheroidal, but they may be branched or even flattened. Their nuclei are round or oval.

The *plasma-cells* (fig. 262, *p. p.*) are distinguished from the lamellar and granular cells by the extreme vacuolation of their cell-substance. The protoplasm between the vacuoles is clear, but may contain a few fine dark granules. The fluid which occupies the vacuoles is presumably of the nature of lymph or blood-plasma: it is less refracting than the substance of the protoplasm. It is not contained in the meshes of a spongioplasmic network but is in distinct vacuoles. These plasma-cells are frequently elongated and they may have short branching processes but they are seldom

[1] Hence termed "eosinophile cells" by some authors. The same term has also been applied by Ehrlich to those leucocytes which have obvious granules, staining with eosin (see p. 213).

or never simply spheroidal like the granular cells. Cells of the same nature but with larger and more conspicuous vacuoles are met with in situations where capillary blood-vessels are about to be formed (see Development of Blood-vessels).

Cells are occasionally observed in areolar tissue in which nothing but a nucleus and a few scattered granules around it are visible (fig. 262, *c*). These are perhaps the remains of corpuscles which are in process of disintegration, but nothing is definitely known as to the removal and regeneration of the cells of connective tissue, nor as to the genetic connection, if any, existing between the several kinds of cells met with in the tissue. The three kinds of cells above described all belong to the so-called "fixed cells" of the connective tissue. The "migratory cells," which are occasionally seen in areolar tissue, are identical with the pale blood- or lymph-corpuscles.

In *areolar tissue* all the varieties of connective tissue cells above described occur. They have no very definite arrangement. Both the cells and the spaces in which they lie may inter-communicate by their branches, and in this way it often happens where the tissue is thicker, that the system of cells and cell-processes, and of corresponding canals, may effect a communication between the superficial and deeper parts of the tissue. The cells of areolar tissue are also connected with the flattened cells which line the smaller blood-vessels and lymphatics, and by means of this connection, and the continuity of the cell-spaces of the tissue, channels are provided for the flow of blood-plasma from the blood-vessels or towards the lymphatics. In addition to this, no doubt some of the plasma or lymph may soak through the ground-substance, or find its way through the lacunar interstices (areolæ) of the tissue.

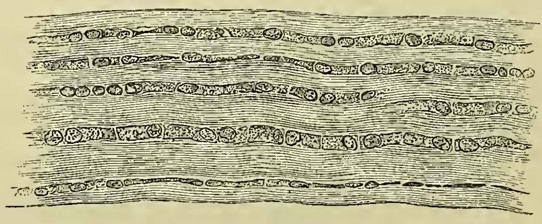


Fig. 271.—Tendon of mouse's tail, stained with logwood; showing chains of cells between the tendon-bundles. 175 diameters. (E. A. S.)

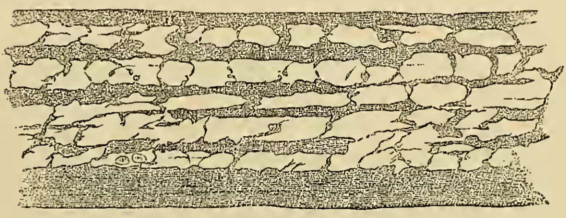
In *fibrous tissue* (tendon and ligament), the cells, which are often called "tendon-cells," are all of the flattened or lamellar variety. They follow the parallel arrangement of the fibre-bundles, and are disposed in rows or chains (fig. 271), which may be easily seen if a very fine tendon, such as those in the tail of the mouse or rat, or a portion only of a larger one is examined under the microscope, and a little dilute acetic acid is cautiously added. A peculiar shape is impressed upon these cells by the close packing of the tendon bundles, for although they may look quadrangular or oblong when the tendon is viewed longitudinally (figs. 271, 274), yet when it is cut across, they have a stellate appearance (figs. 264, 273), for like other flattened connective tissue cells, they send lamellar extensions into the interstices between the contiguous bundles, whilst the middle of each cell, containing the nucleus, lies in the angular space between three or more bundles. When the tendon-cells are viewed longitudinally, any of the lamellar extensions, which are directed either towards or away from the observer, appear as lines on the surface of the cell (fig. 274). The same appearance is often seen upon the flattened cells of the denser forms of areolar tissue, where the cells have been squeezed in between three or more bundles.

Each tendon-cell consists of a delicate protoplasmic body, thicker at the centre and thinning off in the extensions, and containing a flattened, round or oval, clear nucleus, with an intranuclear network and several nucleoli. The ends of adjacent cells are in close apposition, and form, as before noticed, long chains of cells in the tendon, and the nucleus is generally so situated towards one end of the cell as to be

in close proximity to the nucleus of an adjacent cell ; they thus present the appearance of being arranged in pairs (fig. 274). Here and there a third nucleus, with a small amount of protoplasm, may be seen interpolated between two such cells.

The lamellar extensions of the cells do not always end with an even line, but are themselves often prolonged into fine branches, which penetrate still further into the ground-substance which separates the fibre-bundles of the tendon from one another.

In the pure *elastic tissue*, such as that which constitutes the ligamentum nuchæ



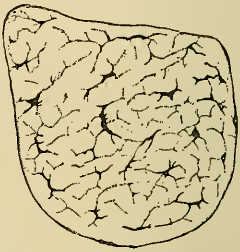


Fig. 272.—Cell-spaces of tendon of mouse's tail, brought into view by treatment with nitrate of silver. 175 diameters. (E. A. S.)

Fig. 273.—Transverse section of tendon of mouse's tail stained with logwood. 175 diameters. (E. A. S.)

The flattened processes of the tendon-cells (which are stained deeply by logwood) appear in section as lines, frequently coming off at right angles from the body of the cell. The bundles of fibres are not represented ; they are very irregular, and but incompletely separated by the cell-processes.

in animals and the ligamenta subflava in man, it is generally stated that cells are altogether absent. Schwalbe finds on the contrary numerous flat connective tissue

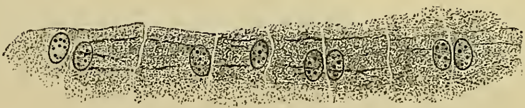


Fig. 274.—Eight cells from the same tendon as represented in fig. 271. Magnified 425 diameters. (E. A. S.)

The nuclei, with their numerous nucleoli, were deeply coloured by the logwood. The dark lines on the surface of the cells are the optical sections of lamellar extensions directed towards or away from the observer.

cells scattered in the ground-substance which lies between the elastic fibres; the cells being often in close apposition with the elastic fibres, but never in continuity with them, as has been described by some authors.

Vessels and nerves.—Blood-vessels, lymphatics, and nerves are everywhere conveyed in the *areolar tissue* to the places where they are to be distributed, but very few blood-capillaries are destined for the tissue itself, although abundant lymphatic networks are present in many parts ; especially in the subcutaneous, subserous and submucous tissues. It is uncertain whether nerves terminate in the areolar tissue. It may be cut in a living animal apparently without giving pain, except when the instrument meets with those branches of nerves which traverse the tissue on their way to other parts.

The *fibrous tissue* receives blood-vessels, but in general they are inconsiderable both in number and size compared with the mass of tissue to which they belong. In tendons and ligaments with longitudinal fasciculi, the chief branches of the vessels run parallel with and between the larger fasciculi, and, sending communicating branches across them, eventually forming a very open network with large oblong meshes. Some fibrous membranes, as the periosteum and dura mater, are much

more vascular ; but the vessels seen in these membranes do not strictly belong to them, being destined for the bones which they cover.

Lymphatics are contained in great abundance, as Ludwig and Schweigger-Seidel showed, in the enveloping areolar-tissue sheaths of tendons and aponeuroses, where they form plexuses with polygonal meshes. In addition to these, a close network of lymphatic vessels with elongated meshes may be injected in the deeper parts of the tendons, where they run in the penetrating areolar tissue. Sometimes, as in the central tendon of the diaphragm, lymphatic spaces separate the tendon bundles from one another. A connection no doubt subsists between these lymphatics and the cell-spaces of the fibrous tissue : and it has been suggested that the lymphatic vessels of the tendons are partly concerned in the removal of lymph from the skeletal muscles, which themselves lack true lymphatic vessels.

The penetrating areolar tissue of tendons, like the same tissue elsewhere, possesses areolæ, which here take the form of elongated clefts, and these may also partly serve for the passage of lymph.

Many tendons and ligaments, and some fibrous membranes, have been shown to possess nerve-fibres, which course for the most part in a direction parallel with the fasciculi and may terminate in a special manner within these tissues, as will be noticed when the peripheral distribution of nerves is described.

As to *elastic tissue*, the yellow ligaments, which contain this in its purest form, are but scantily supplied with blood-vessels, those that are present running in the interstitial areolar tissue between the elastic bundles. The lymphatic vessels also course for the most part longitudinally in the interstitial areolar tissue, being connected here and there by transverse branches, and in addition to these vessels the lymph may be conveyed by means of the elongated areolæ of the same tissue. Neither blood-vessels nor lymphatic vessels actually penetrate into the small bundles of elastic fibres, although the lymphatic vessels often lie close against the surface of the bundles.

ADIPOSE TISSUE.

The human body in the healthy state contains a considerable amount of fatty matter of different kinds. It exists in several of the secretions—in some constituting the chief ingredient ; and it enters into the composition of many of the textures. But by far the greater part of the fat of the body is inclosed in cells of the areolar tissue, which, together with the fibres and blood-vessels which pass between them and serve to bind them together, constitute the adipose tissue.

Distribution.—This tissue is not confined to any one region or organ, but exists very generally throughout the body, accompanying the still more widely distributed areolar tissue in most, though not in all parts in which the latter is found. Still its distribution is not uniform, and there are certain situations in which it is collected more abundantly. It forms a considerable layer underneath the skin, and, together with the subcutaneous areolar tissue in which it is lodged, constitutes in this situation what has been called the *panniculus adiposus*. It is collected in large quantity round certain internal parts, especially the kidneys. It is seen filling up the furrows on the surface of the heart, and imbedding the vessels of that organ beneath its serous covering ; and in various other situations it is deposited beneath the serous membranes, or is collected between their folds, as in the mesentery and omentum, at first generally gathering along the course of the blood-vessels and at length accumulating very copiously. Collections of fat are also common round the joints, lying on the outer surface of the synovial membrane, and filling up inequalities ; in many cases lodged in folds of the membrane, which project into the articular cavity. Lastly, the fat exists in large quantity in the marrow of bones.

On the other hand, there are some parts in which fat is never found in the healthy condition of the body. Thus it does not exist in the subcutaneous areolar tissue of the eyelids and penis, nor in the lungs except near their roots, nor within the cavity of the cranium.

Structure.—When subjected to the microscope, the adipose tissue is seen to consist of small vesicles, filled with an oily matter, and for the most part lodged in the meshes of the areolar tissue. The vesicles are most commonly collected into little lobular clusters (fig. 275), and these again into the little lumps of fat which we see with the naked eye, and which in some parts are aggregated into round or irregular masses of considerable magnitude. Sometimes the vesicles, though grouped together, have less of a clustered arrangement; as when they collect alongside of the minute blood-vessels of thin membranous parts.

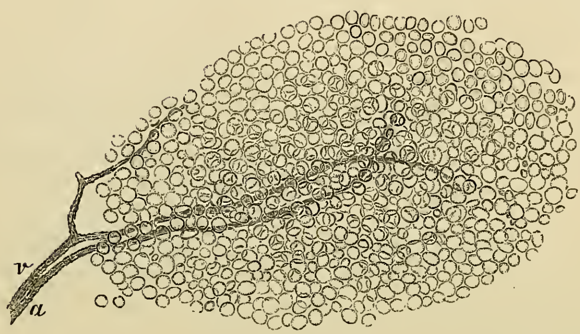


Fig. 275.—A SMALL FAT-LOBULE FROM THE SUBCUTANEOUS TISSUE OF THE GUINEA-PIG, MAGNIFIED ABOUT 20 DIAMETERS. (E. A. S.)

a, small artery distributed to the lobule; *v*, small vein; the capillaries within the lobule are not visible.

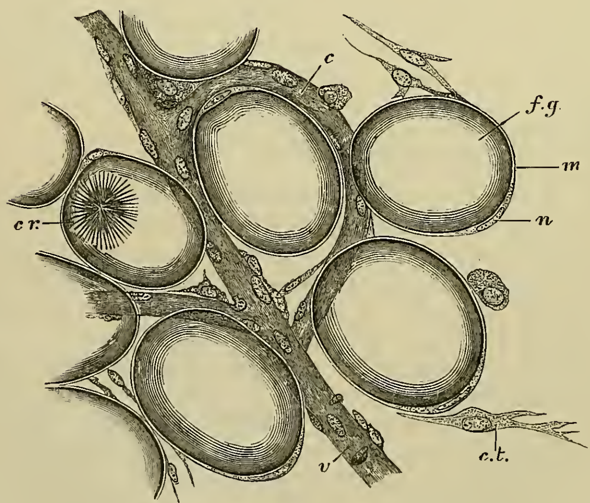


Fig. 276.—A FEW CELLS FROM THE MARGIN OF THE FAT-LOBULE REPRESENTED IN THE PRECEDING FIGURE: HIGHLY MAGNIFIED. (E. A. S.)

f. g, fat globule distending a fat-cell; *n*, nucleus; *m*, membranous envelope of the fat-cell; *c r*, bunch of crystals within a fat-cell; *c*, capillary vessel; *v*, venule; *c t*, connective tissue cell; the fibres of the connective tissue are not represented.

In well-nourished bodies the vesicles or fat-cells are round or oval (fig. 276) unless where packed closely together, in which case they acquire an angular figure, and bear a striking resemblance to the cells of vegetable tissues. The greater number of them are from $\frac{1}{300}$th to $\frac{1}{600}$th of an inch in diameter, but many exceed or fall short of this measurement. Each one consists of a very delicate envelope (*m*), inclosing the oily matter, which, completely filling the envelope, appears as a single drop (*f. g*). It often happens that a part of the fatty contents solidifies in the cell after death, forming a bunch of delicate needle-shaped crystals (fig. 276, *c r*).

The envelope is the remains of the original protoplasm of the cell: it is generally quite transparent, and apparently homogeneous. According to some authorities it

consists of two parts, a delicate structureless external membrane, and a layer of finely granular protoplasm immediately surrounding the fat. The nucleus (*n*) is always present in the protoplasm, but is often so flattened out by the pressure of the inclosed oil-drop as to be visible only with difficulty.

The areolar tissue connects and surrounds the larger lumps of fat, but forms no special envelope to the smaller clusters ; and although fine fasciculi and filaments of that tissue pass irregularly over and through the clusters, yet it is probable that the vesicles are held together in these groups mainly by the fine network of capillary vessels distributed to them. In the marrow the connective tissue fibrils are but few in number or may, it is said, be absent altogether.

The adipose tissue is copiously supplied with **blood-vessels**. The larger branches of these pass into the fat-lumps, where they run between the lobules and

Fig. 277.—Deposition of fat in connective tissue cells of the new-born rat. (E. A. S.)
f, *f′*, fat-cells ; *h*, hæmapoietic cell.

subdivide, till at length a little artery and vein are sent to each small lobule (fig. 275, *a*, *v*), dividing into a network of capillary vessels, which pass between the vesicles in all directions, supporting and connecting them. The **lymphatics** of the fat are in close relation to the blood-vessels, accompanying and occasionally completely enclosing them as they enter the lobule. No nerves have been seen to terminate in this tissue, although

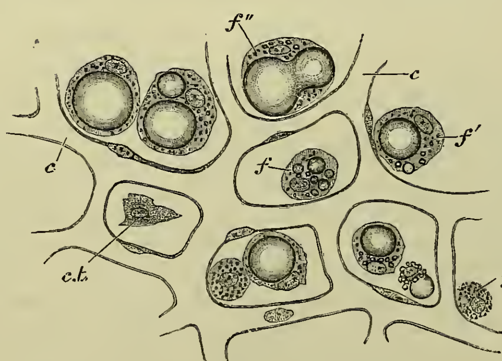


Fig. 278.—Deposition of fat in connective tissue cells. (E. A. S.)
f, a cell with a few isolated fat-droplets in its protoplasm ; *f′*, a cell with a single large and several minute drops ; *f″*, fusion of two large drops ; *g*, granular cell, not yet exhibiting any fat deposition ; *c t*, flat connective tissue corpuscle ; *c*, *c*, network of capillaries.

nerves destined for other textures may pass through it. Accordingly it has been observed that, unless when such traversing nervous twigs happen to be encountered, a puncturing instrument may be carried through the adipose tissue without occasioning pain.

Development.—The fat first appears in the human embryo about the fourteenth week of intra-uterine life. It is deposited in the form of minute granules or droplets in certain cells of the connective tissue (figs. 277, 278, *f*, *f*) : these droplets increase in size, and eventually run together, so as to form one large drop in each cell. By further deposition the cell becomes swollen out to a size far beyond that which it possessed originally, and its protoplasm remains as a delicate envelope surrounding the fat-drop. By the end of the fifth month the fat-cells have largely increased in number, and have become collected into small groups.

The deposit of fat within the cells is preceded and accompanied by the formation of a rich network of capillary blood-vessels (fig. 278), which are produced by a transformation of other cells of the tissue in the manner previously described (p. 218).

The fat is often deposited in the granular cells of the connective tissue, these

being usually found in great abundance in those situations in which fat is becoming developed (fig. 278). Sometimes, however, the deposition takes place in the flattened connective tissue cells (fig. 277, *f*), or in cells which are apparently intermediate between these and the granular cells, being rounded like the latter, but consisting of a much clearer protoplasm (fig. 277, *f′*). When deposited in ramified or flattened cells these acquire a spherical shape as they enlarge, in consequence of the distension produced by the accumulating fat.

The fat in some parts, and especially in the serous membranes, is formed at the expense of pre-existing lymphatic tissue, the lymphoid cells probably becoming enlarged and transformed into fat-cells, whilst a considerable development of blood-vessels accompanies the change. A similar transformation is also witnessed in the thymus gland, which, in the fœtus and infant, is chiefly composed of lymphoid tissue, but as growth proceeds becomes wholly converted into a mass of fat.

The superficial resemblance which adipose tissue often bears to many glands, in its lobulated structure and the arrangement of its blood-vessels, has led some histologists to look upon the fat-cell as a corpuscle of specific nature, and totally distinct from any other kind of cell met with in the connective tissue. But against this view it may be urged that the situations in which fat is deposited are, previously to its appearance, in no way distinguishable from the rest of the areolar tissue ; that the cells in which it is produced are, so far as can be seen, the same as those which are met with in almost all parts of the areolar tissue ; and further, that when from any natural cause the fat is entirely removed from the cells of a part and not again deposited in them, the part eventually acquires all the ordinary characteristics of the areolar tissue. The great development of blood-vessels in adipose tissue is obviously related to the function which it subserves in storing up the fatty materials derived from the food in such a form and situation as to be readily re-absorbed into the circulation when needed. Fat may be deposited in other cells besides those of connective tissue.

PIGMENT.

An accumulation of coloured pigment-granules is met with in many cells of the animal body, but most frequently in epithelium-cells and in cells belonging to the connective tissue. A well-marked example of pigmented epithelium-cells in the human body is afforded by the black coating which forms the external layer of the retina of the eye, and covers the posterior surface of the iris. Pigment is also met with in the deeper layers of the cuticle, especially in the coloured races, in the cortical substance of the hairs, in certain epithelial cells of the membranous labyrinth of the ear, and the olfactory region of the nose.

In the connective tissue the pigment is met with in enlarged and irregularly branched corpuscles which are termed **pigment-cells.** Such ramified cells are very common in many animals. In the human body cells of this description are found in the dark tissue on the outer surface of the choroid coat (fig. 279), in the iris, where they are often variously coloured, and on the pia mater covering the upper part of the spinal cord. Pigment is also found in some of the ramified cells which form part of the retiform tissue of the medullary substance of lymphatic glands, and occasionally in some of the similar cells of the spleen. It may also be seen in migratory cells, and these are believed to carry the pigment to the epithelial structures in which it is deposited.

The pigment (melanin) which is contained within the cells, consists of black or brown granules or molecules of a round or oblong shape, and almost too small for exact measurement. These molecules are densely packed together in some cells ; in others they are more scattered, and then it may be seen that there is a certain amount of colourless matter included along with them. When they escape from the ruptured cells, they exhibit very strikingly the " Brownian " molecular movement ; and in consequence of this movement the apparent figure of the particles is subject to change. It is worthy of remark, that when viewed singly with a very high magnifying power they look transparent and almost colourless, and it is

only when they are heaped together that their dark colour distinctly appears. The nucleus of the pigment-cell is not coloured, but is very often hidden from view by the black particles.

In the lower animals remarkable movements are often observed in the ramified pigment-cells, *e.g.*, those of the frog's skin. In these the dark particles of pigment

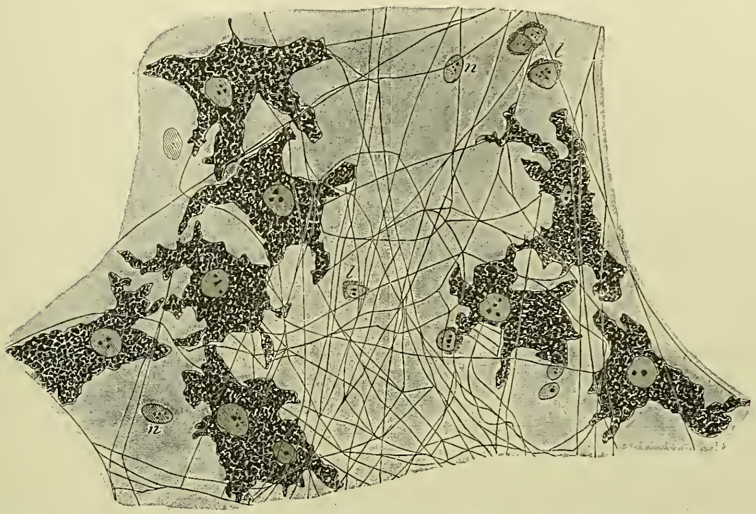


Fig. 279.—A SMALL PORTION OF THE CHOROID COAT OF THE EYE : HIGHLY MAGNIFIED. (E. A. S.)
p, pigment-cells ; *f*, elastic fibres ; *n*, nuclei of epithelioid cells (the outlines of the cells are not indicated) ; *l*, lymphoid cells.

are at one time dispersed through the whole cell and its branches, but at another time they gather into a heap in the central part, leaving the rest of the branched cell vacant, but without alteration of its figure. In the former case the skin is of a dusky hue ; in the latter, pale. The aggregation of the pigment-molecules can be excited through the nerves, both directly and also in a reflex manner, as by the stimulus of light upon the retina.

RETIFORM OR RETICULAR TISSUE.

This is a distinct variety of connective tissue which is met with widely distributed in various parts of the body, constituting the whole framework of some organs and entering largely into the constitution of many mucous membranes. It is composed of a very fine network or reticulum of connective-tissue fibrils, which in their behaviour to staining reagents and in their general microscopic appearance closely resemble the white fibres of areolar tissue, with which, in the lymphatic glands, they are undoubtedly continuous. In their chemical character they are, according to Mall, more nearly allied to elastic fibres, or rather with the membranes of the elastic fibres. However this may be, it is nevertheless clear from its anatomical continuity with the white fibrils of connective tissue that the retiform tissue is merely a variety of areolar tissue, being formed of very fine anastomosing bundles, with the meshes of the network occupied by fluid ; the ground substance having disappeared. In most situations the fixed cells of the tissue are applied to and are wrapped round the strands of the network, which may thus be in great measure concealed by the cells. The tissue then appears formed of a network of branching and anastomosing cells, and was for a long time so described, but if the cells are brushed away or

otherwise removed, as by a short treatment with dilute alkali, the fibres of the reticulum come clearly into view (figs. 280, 281). The true structure of this tissue was first pointed out by Bizzozero.

In many situations the meshes of the retiform tissue are occupied by numerous corpuscles which closely resemble the pale blood- or lymph-corpuscles, but have a relatively larger nucleus, and less protoplasm than those. They are known as *lymphoid cells,* and the tissue containing them is termed **lymphoid or adenoid tissue.** This tissue is found composing the greater part of the lymphatic glands, and other structures allied to them, such as the solitary and agminated glands of the intestine, and the similar structures in the tonsils and elsewhere. Moreover, the alimentary mucous membrane is in some parts composed of the same tissue, and it occurs also in other mucous membranes and, in the form either of elongated tracts or of isolated nodules, in many parts of the serous membranes. In the spleen, the interstices of the retiform tissue are for the most part occupied by blood, instead of by lymph as elsewhere. In organs into the construction of which this tissue enters, it serves as a supporting framework to those parts of the organ into which connective tissue of the ordinary kind does not penetrate.

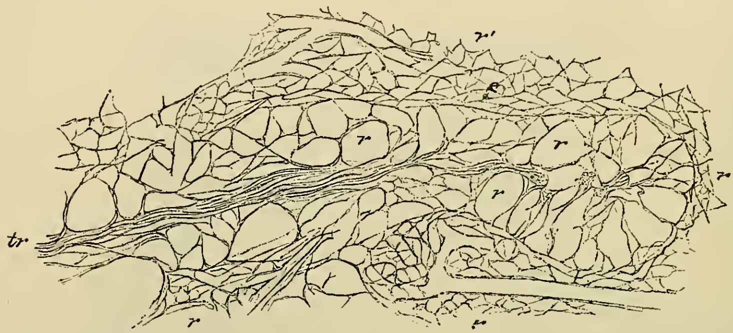


Fig. 280.—Reticulum from the medullary part of a lymphatic gland. (E. A. S.)

tr, end of a trabecula of fibrous tissue ; *r*, *r*, open reticulum of the lymph-path, continuous with the fibrils of the trabecula ; *r'*, *r'*, denser reticulum of the medullary lymphoid cords. The cells of the tissue are not represented, the figure being taken from a preparation in which only the connective tissue fibrils and the reticulum are stained.

Fig. 281.—End of a fibrous trabecula from the same preparation, showing the continuity of the connective tissue fibrils with the reticulum: highly magnified. (E. A. S.)

tr, trabecula ; *r*, reticulum.

DEVELOPMENT OF CONNECTIVE TISSUE.

Those parts of the early embryo in which connective tissue is subsequently to be developed, are at first composed entirely of embryonic cells, to all appearance similar to those which constitute the mesoblastic layer generally. It is, however, believed by many authorities that in their origin the cells which form the connective

tissues and the vessels are esentially different from those which produce the other tissues, and that they have wandered in between the other cells of the mesoblast from the peripheral part of the blastoderm (parablast-cells of His, mesenchyme cells of Hertwig. *See* Embryology, pp. 25-27).

The mesoblast cells which are concerned in the formation of the connective tissues are at first rounded in shape, and loosely packed, and exhibit amœboid movements when examined on the warm stage. Subsequently they become irregularly ramified and tend to unite with one another so as to form a kind of cell-network with open interstices. These interstices are at first occupied by an albuminous fluid which later acquires a mucous or muco-albuminous character and becomes more consistent : it may now be spoken of as the ground-substance or matrix.

In this ground-substance fibres become developed of the two kinds, white and elastic, but the manner in which they are formed is by no means clear ; and two distinct and opposed views are held by histologists upon the subject. According to the one view, the bundles of white fibrils are produced by a direct conversion of the protoplasm of some of the cells, the others remaining as the permanent connective tissue corpuscles ; or the permanent corpuscles represent embryonic cells, layers of whose protoplasm have been successively converted into fibrillar tissue, the cells, meanwhile, after each such conversion, growing again to their original size,

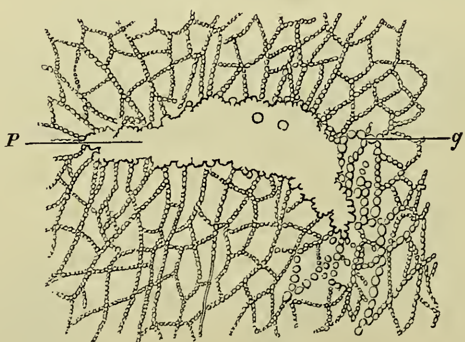


Fig. 282.—Development of elastic tissue by deposition of fine granules. (Ranvier.)

g, moniliform fibres formed of rows of "elastin" granules ; *p*, flat platelike expansion of elastic substance formed by the fusion of "elastin" granules.

and at length remaining in contact with the bundle of fibres which they have assisted to form. Similarly the elastic fibres are believed to be formed of the processes of some others of the embryonic cells, which become connected with processes of neighbouring cells, and undergoing a chemical transformation, produce the networks of elastic fibres. According to the other view the fibres, both white and elastic, are formed by a deposit in the intercellular substance, and not by a direct change of the protoplasm of the cells, with which indeed they are not connected ; although it is not excluded that the deposition may in some way or other be influenced, or even caused by the pre-existing cells.

In favour of the former view is the fact that in young connective tissue there are sometimes to be seen long cells with fibrillated protoplasm which might be regarded as in process of conversion into bundles of white fibrils. And various authors have described an apparent continuity both in young and in developed connective tissue of the elastic fibres with the cells of the tissue, or even with their nuclei.

In favour of the latter view may be instanced the appearance of the jelly-like connective tissue of the early embryo in which the fibres of both kinds can be seen coursing through the jelly-like intercellular substance, apart entirely from the cells. In the case of the elastic fibres, these, as shown by Ranvier, appear in the form of rows of granules or globules, which subsequently become fused together end to end, and are not at any time continuous with cells (fig. 282). To form an elastic membrane, in place of being arranged in lines the globules are deposited in small patches.

and by their fusion the membrane is formed (p). In elastic cartilage the granules first make their appearance, it is true, in the immediate neighbourhood of the cartilage-cells; but although this renders it probable that the deposition of the granules is influenced by the cells, it does not prove that they are formed by a direct conversion of the cell-protoplasm. Indeed, the subsequent extension of the fibres into those parts of the matrix which were previously clear of them (a process which can be easily followed in the arytenoid cartilage of the calf), and in which no such direct conversion of cell protoplasm seems possible, is a strong argument in favour of the deposition hypothesis.

The view which supposes that a direct conversion of the protoplasm of the connective tissue cells takes place into fibres, both white and elastic, has of late years been widely adopted, but it seems to rest largely upon a desire to interpret the facts in accordance with the conception (originally formulated by Beale and M. Schultze), according to which every part of an organised body consists either of protoplasm (formative matter), or of material which has been protoplasm (formed material); the idea of a deposition or change occurring outside the cells in the intercellular substance being excluded. It is, however, not difficult to show that a formation of fibres may occur in the animal organism without a direct transformation of protoplasm, although the materials for such formation may be furnished by cells. Thus in those cœlenterates in which a low form of connective tissue first makes its appearance, this is distinguished by a total absence of cellular elements, a ground-substance only being developed and fibres becoming formed in it. Again, the fibres of the shell-membrane of the bird's egg are certainly not formed by the direct conversion of the protoplasm of the cells which line the oviduct, although they are formed in matter secreted by those cells, and it is through their agency that the deposit occurs in a fibrous form.

In the formation of retiform tissue the ground-substance appears to become entirely liquefied except where it enters into the composition of the reticulum, and the cells of the tissue become applied to the anastomosing fibril bundles, and by their union constitute a network of branched cells enveloping the network of fibrils.

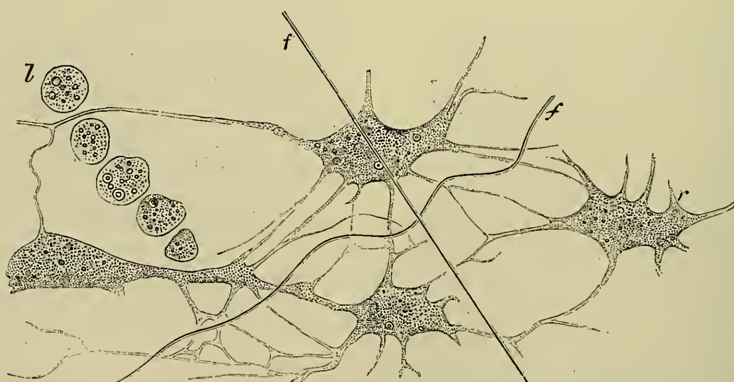


Fig. 283.—Jelly of Wharton. (Ranvier.)

r, ramified cells intercommunicating by their branches; l, a row of leucocytes or migratory cells; f, f, fibres coursing through the ground-substance.

In lymphoid tissue the meshes become occupied by lymph corpuscles which may originally have come from the blood or lymphatic vessels, but afterwards multiply by cell-division.

The jelly-like connective tissue of the early embryo persists in the umbilical cord until birth as the so-called jelly of Wharton (fig. 283). Elsewhere it has largely lost its jelly-like character in consequence of the development of fibres in the ground-substance, but the amount to which they are developed varies greatly in

different animals, and in the connective tissues of different parts. In the vitreous humour of the eye no fibres are developed, and the cells become for the most part either atrophied or much modified, and remain relatively few in number. The so-called *jelly-like connective tissue* which is thus produced consists therefore almost entirely of ground-substance.

Connective tissue appears to be readily regenerated, although the new cicatricial tissue which is formed in place of that which has been removed by the knife or by disease, is not always obviously of the same character, either as regards its cells or fibres, as the tissue it replaces.

As to the mode of its regeneration there is still some uncertainty. It was believed by Cohnheim, whose views have been supported by the experiments of Ziegler, that the new tissue was formed by the leucocytes (lymph-corpuscles) of the granulation tissue which first appears in the wound. But it is affirmed on the other hand by other observers that the leucocytes, although unquestionably the precursors of the newly-forming tissue, do not take any direct part in its formation, but are gradually replaced by plasma-cells of the surrounding tissue which also wander into the space within which the new tissue is to become formed. Here they produce the cicatricial tissue, either by immediate transformation of their protoplasm into fibrils, or by an extracellular formation in the adjacent ground-substance.

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CARTILAGE.

This is the well-known substance commonly called "gristle." The following are its more obvious characters. When in mass, it is opaque and of a pearly or bluish white colour, in some varieties yellow; but in thin slices it is translucent. Although it can be easily cut with a sharp knife, it is nevertheless of very firm consistence, but at the same time highly elastic, so that it readily yields to pressure or torsion, and immediately recovers its original shape when the constraining force is withdrawn. By reason of these mechanical properties, it serves important purposes in the construction of some parts of the body.

In the early embryo the skeleton is, in great part, cartilaginous; but the cartilage forming its different pieces, which have the outward form of the future bones, in due time undergoes ossification or gives place to bone, in the greater part of its extent at least, and hence this variety of cartilage is named "temporary."

Of the permanent cartilages a great many are in immediate connection with bone, and may be still said to form part of the skeleton. The chief of these are the articular and the costal cartilages; the former cover the ends or surfaces of bones in the joints, and afford these harder parts a thick springy coating, which breaks the force of concussion and gives ease to their motions; the costal or rib-cartilages form a considerable part of the solid framework of the thorax, and impart elasticity to its walls. Other permanent cartilages enter into the formation of the external ear, the nose, the Eustachian tube, the larynx, and the windpipe. They strengthen the substance of these parts without undue rigidity; maintaining their shape, keeping open the passages through them where such exist, and giving attachment to moving muscles and connecting ligaments.

Cartilages, except those of the joints, are covered externally with a moderately vascular fibrous membrane named the *perichondrium.*

When a very thin slice of cartilage is examined with the microscope, it is seen to consist of nucleated cells, disseminated in a solid mass or matrix (fig. 285). The matrix is sometimes transparent, and to all appearance homogeneous; sometimes dim and very faintly granular, like ground glass: both these conditions occur in *hyaline cartilage,* which may be regarded as the most typical form of the tissue. Two varieties exist in which the matrix is pervaded to a greater or less extent by fibres. In the one, named *elastic* or *yellow fibro-cartilage,* the fibres are similar to those of elastic tissue; in the other, named *white fibro-cartilage,* they are of the white kind as in ordinary ligament.

HYALINE CARTILAGE.

Structure.—In hyaline cartilage the matrix, as just stated, is uniform, and, when examined fresh, usually appears free from fibres. Like the ground-substance or matrix of connective tissue, it becomes stained brown by nitrate of silver and subsequent exposure to the light. The cells consist of a rounded, oval, or bluntly angular *cell-body* of translucent protoplasm, embedded in which are fine curvilinear interlacing filaments and minute granules (fig. 284), with a round *nucleus,* which is either clear with one or more *nucleoli,* or, more commonly, is occupied by a network of chromoplasm, which produces under a low power of the microscope a granular effect. The cell-body lies in a cavity of the matrix, which, in its natural condition, it entirely fills. This cavity is bounded and inclosed by a transparent *capsule,* which is seldom obvious to the eye, for it coheres intimately with the surrounding matrix, with which it agrees in nature, and cannot usually be distinguished without the aid of re-agents.

By exposure to water and some other liquids, as well as to the action of electric shocks, the cell-body shrinks away from the inside of the capsule, and assumes a jagged or otherwise irregular figure, and then may hide the nucleus (fig. 287). It often contains larger or smaller fat-globules (fig. 285, *g*).

The cells of cartilage appear to contain glycogen, for they are coloured reddish brown by iodine (Neumann).

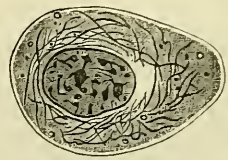


Fig. 284.—A CARTILAGE CELL IN THE LIVING STATE, FROM THE SALAMANDER: HIGHLY MAGNIFIED. (Flemming.)

They are rarely dispersed singly in the matrix; most commonly occurring in groups of two or more. When disposed in pairs (as at *a*, fig. 285) the cells are generally triangular or pyramidal in form with rounded angles, and with their bases opposite one another; in the larger groups (*b*) the cells have a straight outline where they adjoin or approach one another, but at the circumference of the group their outline is rounded. Towards the surface of the cartilage the groups are generally flattened conformably with the surface, appearing narrow and almost linear when seen edgeways, as in a perpendicular section (fig. 286, *a*).

Various observers, and especially Tillmanns, have shown that the matrix of hyaline cartilage can be broken up after long maceration, and with the aid of pressure, into fine fibrils. According to Cresswell Baber, these fibres are vertical to the surface in articular cartilage, and parallel with the long axis in rib cartilage. They are more easily seen in the cartilage of birds than of mammals. Their chemical nature is not very clear, nor is it certain how far the appearances correspond with any structure naturally present; but if, as Kühne and Merochowetz assert, gelatin and mucin can be obtained from the matrix of cartilage, the fibres in question may be chemically of the same nature as the white fibres of connective tissue, the mucin belonging to the ground-substance in which they are embedded.

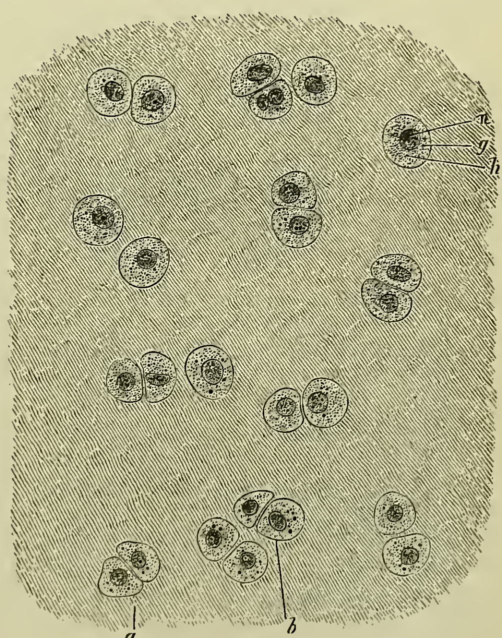


Fig. 285.—ARTICULAR CARTILLAGE FROM HEAD OF METATARSAL BONE OF MAN (OSMIC ACID PREPARATION). THE CELL-BODIES ENTIRELY FILL THE SPACES IN THE MATRIX. 340 DIAMETERS. (E. A. S.)

a, group of two cells; *b*, group of four cells; *h*, protoplasm of cell, with *g*, fatty granules; *n*, nucleus.

Other histologists have described a network of exceedingly fine ramified canals penetrating the cartilage-matrix, and effecting a communication between the cell-spaces. Up to the present time, however, the existence of such anastomosing channels has not been conclusively proved, although often assumed in order to explain the manner in which nutritive plasma penetrates the matrix of cartilage to reach the cells. Budge endeavoured to demonstrate the existence of canaliculi by forcing coloured injecting fluid into the substance of cartilage, but the result of the experiment was not conclusive. It has also been attempted to show them by the so-called natural method of injection, that is by allowing indigo-carmine (which has an

intensely blue colour) to mix with the circulating blood of animals, which after a time are killed and the cartilages examined. Proceeding in this way, Gerlach was unable to see any blue channels in the cartilage-matrix, while Arnold, on the other hand, obtained results from which he was led to infer the existence of minute cleft-like spaces throughout the matrix, connected by fine radiating canaliculi on the one hand with the lymphatics in the perichondrium, and on the other hand with the cell-spaces of the cartilage.

Such is the structure of hyaline cartilage in general, but it is more or less modified in different situations.

In **articular cartilage**, the matrix in a thin section appears dim, like ground glass, having sometimes an almost granular aspect. The cells and cell-groups are smaller and more dispersed, as a rule, than in rib-cartilage. As is the case also with the cartilage of the ribs, the groups are flattened at and near to the surface, and lie

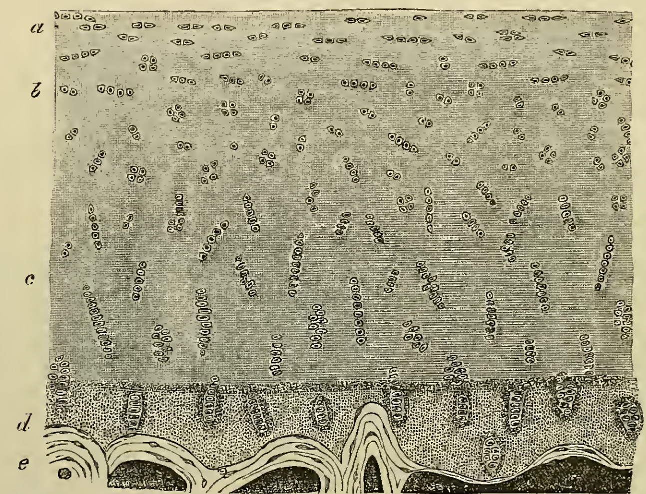


Fig. 286.—Vertical section of articular cartilage covering the lower end of the tibia (human). Magnified about 30 diameters. (E. A. S.)

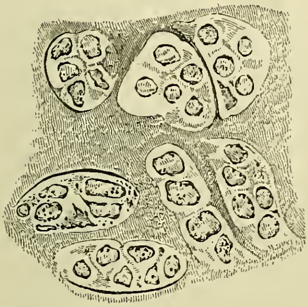
a, cells, and cell-groups flattened conformably with the surface ; *b*, cell-groups irregularly arranged ; *c*, cell-groups disposed perpendicularly to the surface ; *d*, layer of calcified cartilage ; *e*, bone.

parallel with it (fig. 286, *a*) ; deeper and nearer the bone, on the other hand, they are narrow and oblong, like short irregular strings of beads, and are mostly directed vertically (fig. 286, *c*). It is well known that articular cartilages readily break in a direction perpendicular to their surface, and the surface of the fracture appears to the naked eye to be striated in the same direction, as if they had a columnar structure ; this may be due to the vertical arrangement of the rows of cells, or to the substance of the matrix being disposed in a fibrous or columnar manner (Leidy). It was formerly held that the free surface of articular cartilage is covered with epithelioid cells, but no such covering really exists. It is easy, no doubt, to peel off a thin film from the surface of the cartilage of the head of the humerus or femur ; but this superficial layer is really part of the cartilage, and its broad patches of cells with the intermediate matrix are not to be mistaken (fig. 287).

Near the margin of the articular cartilages connective tissue is prolonged a certain way into them from the periosteum and synovial membrane, and the cartilage-cells acquire processes and present transitions to the connective-tissue corpuscles of that membrane (fig. 288). There is no sharp demarcation between the two tissues, which here pass continuously into one another.

Except at this transitional zone the matrix of articular cartilage rarely

becomes converted into fibro-cartilage, nor is it prone to ossify like rib-cartilage. But a deposit of calcareous granules may occur in the deeper parts of the articular cartilage near the bone, the deposit first showing itself around the



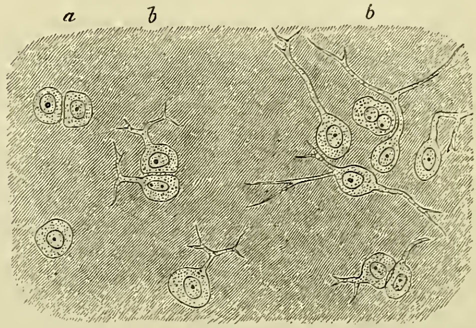


Fig. 287.—A thin layer peeled off from the surface of the cartilage of the head of the humerus, showing flattened groups of cells (Sharpey).

The shrunken cell-bodies are distinctly seen, but the limits of the capsular cavities where they adjoin one another are but faintly indicated. Magnified 400 diameters.

Fig. 288.—Border of articular cartilage showing transition of cartilage cells into connective-tissue corpuscles. From head of metatarsal bone (human). About 340 diameters. (E. A. S.)

a, ordinary cartilage cells ; *b*, *b*, with branching processes.

groups of cartilage cells (fig. 286, *d*). This change may also happen at the symphyses. When the earthy matter is extracted by means of an acid, the tissue which remains has all the characters of cartilage.

In the **costal cartilages**, the cells, which are of considerable size, are also collected in groups, larger for the most part than those found in articular cartilage (fig. 289). Near the exterior of the cartilage they are flattened, and lie parallel with

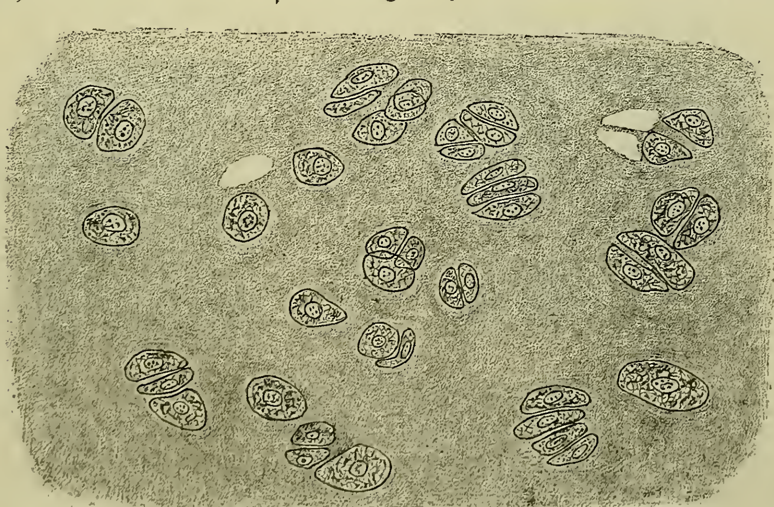


Fig. 289.—From a section of costal cartilage from the calf. Chromic acid preparation (E. A. S.).

The matrix is indistinctly fibrous. Two or three empty cell-spaces are seen in the section, the cells having dropped out. The cell-protoplasm is reticular.

the surface. As to those situated more inwardly, we can sometimes observe, in a transverse slice, that they form oblong groups disposed in lines radiating to the

circumference ; but this arrangement is not constant, and they often appear quite irregular. The cells, with the exception of those lying upon the surface, frequently contain drops of oil, the nucleus being often altogether concealed by the fat. The matrix is clear, except where fibres have been developed in it, in which parts it is opaque and yellowish. Such fibrous patches are very frequent ; the fibres are fine, straight, and parallel, appearing transparent when few together. Besides these fibrous patches in the interior of the rib-cartilages, the subperichondral layer is also pervaded by bundles of fibres which are directly prolonged from the fibre-bundles of the perichondrium and gradually lose themselves in the cartilage-matrix. There is in fact no sharp line of demarcation between the perichondrium and the subjacent cartilage, the one tissue passing by imperceptible gradation into the other. There is indeed reason to believe that the superficial layers of the cartilage are formed by a transformation of the fibrous tissue of the perichondrium during the growth of cartilage. It is not uncommon to find the rib-cartilages extensively ossified.

The description given of the microscopic characters of the costal cartilages will apply with little variation to the ensiform cartilage of the sternum, to the cartilages of the larynx and windpipe, except the epiglottis and cornicula laryngis, and to the cartilages of the nose. With the exception of the last, these resemble the rib-cartilages also in their tendency to ossify.

The characters of the temporary cartilages, which are hyaline, will be noticed in the account of the formation of bone.

ELASTIC OR YELLOW CARTILAGE.

The epiglottis and cornicula of the larynx, the cartilages of the ear and of the Eustachian tube, differ so much from the foregoing, both in intimate structure and outward characters, that they have been included in a class apart, under the name of the "elastic," "yellow," or "spongy" cartilages. These are opaque and somewhat

Fig. 290.—Section of the elastic cartilage of the ear. Highly magnified (Hertwig).

Fig. 291.—Section of part of the cartilage of the epiglottis (Ranvier).

a, cartilage cell in clear area ; *b*, granular-looking matrix near the middle of the cartilage, the granular appearance being due partly to the fine reticulum of elastic fibres, partly to the presence of granules of elastic substance in the matrix ; *c*, clearer matrix with longer fibres.

yellow, are more flexible and tough than the ordinary cartilages, and have little tendency to ossify. They are made up of cells and a matrix, but the latter is everywhere pervaded with fibres (fig. 290), except in a small area or narrow zone left round each of the cells. The fibres resist the action of acetic acid ; they are in many parts short, fine, and confusedly intersecting each other in all directions, like the

filaments in a piece of felt; in such parts the matrix has a rough indistinctly granular look, but sometimes this appearance is due to the fact that the elastic fibres are incompletely developed, the granules which are to form them having not yet run together into fibres. Sometimes the fibres are longer (fig. 291, *c*) but they still intercommunicate at short distances.

In large animals such as the ox, where the fibres of ordinary elastic tissue attain a considerable size, those of elastic cartilage are also very large with comparatively wide meshes, occupied of course by the hyaline ground-substance.

WHITE FIBRO-CARTILAGE.

This is a substance consisting of a mixture of the fibrous and cartilaginous tissues, and so far partaking of the qualities of both. Like hyaline cartilage, it possesses firmness and elasticity, but these properties are united with a much greater degree of flexibility and toughness. It presents itself under various forms, which may be enumerated under the following heads :—

1. *Interarticular disks.* These are interposed between the moving surfaces of bones, or rather of articular cartilages, in several of the joints. In the joint of the lower jaw and in that of the clavicle they have the form of round or oval plates, growing thinner towards the centre ; in the knee-joint they are curved in form of a sickle, and thinned away towards their concave free edge. In all cases their surfaces are free ; while they are fixed by synovial or fibrous membrane at their circumference or extremities. The synovial membrane of the joint is prolonged for a short distance upon these fibro-cartilages, from their attached margin.[1]

2. The articular cavities of bones are sometimes deepened and extended by means of a rim or border of fibro-cartilage. Good examples of these *marginal fibro-cartilages* are seen in the shoulder and hip-joints, attached round the lip of the articular sockets. In the joint of the lower jaw, the cartilage lining the glenoid cavity is also largely fibrous.

3. *Connecting fibro-cartilages* are such as pass between the adjacent surfaces of bones in joints which do not admit of gliding motion, as at the symphysis of the pubis and between the bodies of the vertebræ. They have the general form of disks, and between the vertebræ are composed of concentric rings of fibrous tissue with cartilage-cells and matrix interposed ; the fibrous tissue predominating at the circumference, the cartilaginous tissue increasing towards the centre. The bony surfaces which they connect are usually encrusted with true cartilage.

4. The bony grooves in which tendons of muscles glide are lined with a thin layer of fibro-cartilage. Small nodules of this tissue (*sesamoid fibro-cartilages*) may also be developed in the substance of tendons, of which there is an example in the tendon of the peroneus longus, and also in that of the tibialis posticus, where it passes beneath the head of the astragalus.

Fibro-cartilage appears under the microscope to be made up of wavy fibres, like those of ordinary ligament, with cartilage-cells occupying the place, and often simulating the arrangement, of the tendon-cells. As in elastic fibro-cartilage, the cells are immediately surrounded by a part of the matrix which is free from fibres (fig. 292). As a general rule they resemble the cells of ordinary cartilage, having a rounded shape, although somewhat flattened where the bundles of fibres are closely packed.

[1] It has been stated by several authors that the interarticular disks are formed of fibrous tissue only, without any intermixture with cartilage. This statement is, however, incorrect. In all cases (jaw, clavicle and knee), there are unmistakeable rows and groups of cartilage-cells enclosed in capsules, between the bundles of white fibres.

In the intervertebral fibro-cartilages, many of the cartilage-cells are provided with long and ramified processes that extend far beyond the body of the cell.

The proportion which the fibrous bundles bear to the true cartilage, differs much in different examples of this tissue. In general the fibrous tissue very greatly predominates, and in some cases, as in the interarticular laminæ of the knee-joint, it

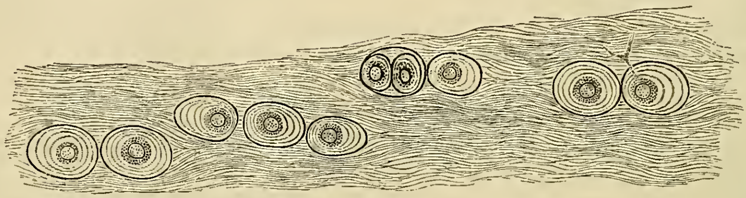


Fig. 292.—White fibro-cartilage from an intervertebral disk (human). Highly magnified. (E. A. S.)

The concentric lines around the cells indicate the limits of deposit of successive capsules. One of the cells has a forked process which extends beyond the hyaline area surrounding the cell, amongst the fibres of the general matrix.

constitutes almost the entire structure, but cartilaginous tissue with characteristic cells predominates near the surfaces. In the intervertebral disks the cartilage-corpuscles are, as already stated, more abundant towards the central pulp than near the periphery, but the centre of the pulp itself does not contain cartilage-cells, but a reticulated cell-structure embedded in soft matrix, derived from the cells of the chorda dorsalis of the embryo. In all the symphyses the cartilage which is in immediate contiguity with the bony surfaces is hyaline.

In the healthy state, no blood-vessels penetrate the articular cartilages. Whatever nutrient fluid they require seems to be derived from the vessels of adjoining textures, especially the bone, and to be conveyed through the tissue by imbibition. Towards the circumference of the cartilage, however, underneath the synovial membrane, the synovial vessels form a narrow vascular border round it, which has been named the *circulus articuli vasculosus.*

When the tissue exists in thicker masses, as in the cartilages of the ribs, canals are here and there excavated in its substance, along which vessels are conducted for the nourishment of the parts too distant to receive it from the vessels of the perichondrium. But these canals are few and wide apart, and the vessels do not pass beyond them to ramify in the intermediate mass, which is accordingly quite extravascular. Besides blood-vessels these canals usually contain a number of cells resembling lymph-corpuscles, a few connective tissue corpuscles and even in places some connective tissue fibres. The contents of the canals are sometimes spoken of as "cartilage-marrow." The cartilage cells in the immediate neighbourhood of the canals are disposed as at the surface of the cartilage, *i.e.*, they are flattened conformably to the wall of the canal.

No nerves have been traced into any of the cartilages, and they are known to be destitute of sensibility.

The matrix of cartilage is converted after long boiling into a substance termed chondrin which gelatinizes on cooling. This may be due however to its containing gelatine (see p. 245).

DEVELOPMENT OF CARTILAGE.

The parts of the embryo which are to become cartilages are made up at first of the common mesoblastic cells from which the connective tissues generally originate. After a time the cell-contents become clearer, the nucleus more visible, and the cells, mostly of polygonal outline, appear surrounded by clear lines of

pellucid substance, forming as it were a network of bright meshes inclosing them, but in reality consisting of the cohering capsules of the contiguous cells, and constituting all that exists of the matrix at this time.[1] Glycogen appears at an early period in the protoplasm of cartilage-cells. Rouget found it in the sheep's embryo of two months, both in ossifying cartilage and in the cartilages of the trachea.

The subsequent changes consist in enlargement and multiplication of the cells and development of the intermediate matrix from a substance which is formed around and between them. The process appears to be as follows (fig. 293) :—The cartilage cells first divide, a species of capsule being formed round each of the young cells (B), whilst the old one inclosing them becomes blended with the intercellular matrix, and after a time, is no longer traceable (C). The new cells, in turn, divide in the same way, so as to make a group of four, each of which is surrounded by its own capsule (D), whilst the capsules of the first descent (secondary) blend with the matrix (E) like their predecessor.

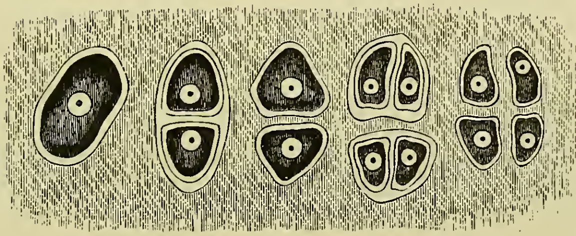


Fig. 293.—Plan of the multiplication of cells of cartilage (Sharpey).

A, cell in its capsule ; B, divided into two, each with a capsule ; C, primary capsule disappeared, secondary capsules coherent with matrix ; D, tertiary division ; E, secondary capsules disappeared, tertiary coherent with matrix.

The four cells may each form a succession of capsules and thus become more separated from one another, or they may divide again and form a group of eight or more. It is by reason of the cells remaining in contiguity with one another after the division is complete that the groups of corpuscles which are so characteristic of cartilage are produced.

It is doubtful how the capsule is produced ; whether excreted by the cell which it afterwards incloses, as held by Kölliker; or formed by conversion of a superficial layer of the protoplasm of the cell-body, as was taught by Max Schultze ; or a primarily independent deposit around the cells. However this may be, there is at first no matrix but what is made up of the simple capsules.

In further growth there is a difference, according as the cells do or do not undergo frequent division. In the latter case a cell becomes surrounded by many concentric capsules formed in succession ; that is, the first capsule is expanded, and the others formed each within its expanding predecessor, so that the cartilage comes to consist of scattered cells, each with a concentric system of capsules, which by means of re-agents may be rendered visible in the neighbourhood of the cells, but further off are inseparably blended into a uniform substance. When, on the other hand, the cells have a tendency to frequent subdivision, the new capsules are produced by the new cells, and are included in and finally blend with those which had belonged to the previous cells, as shown by fig. 293.

[1] Cartilages, which retain this condition throughout life, have been termed "parenchymatous." An example of this is found in the cartilage of the mouse's ear.

The matrix, although thus formed of the capsules, usually becomes to all appearance homogeneous ; but in sections of cartilage that have been exposed to acids and other re-agents, the contour lines of the capsules round cells and cell-groups may be more or less distinctly brought into view.

The mode in which the division of the cartilage-cell takes place has been carefully studied by Schleicher, and the stages of the process followed in the living tissue (fig. 294). The nuclear membrane first of all disappears, or is converted into filaments of chromoplasm. These become lost amongst the other filaments which result from the conversion of the nucleoli and other more solid contents of the nucleus. The filaments are at first short and irregular (*a*), and soon take on a stellate arrangement (*b*). After a time they become grouped in a parallel manner in the centre of the nucleus (*c,d*). The parallel fibres soon divide into two groups, which pass towards the poles of the nucleus. Sometimes the gap between the groups is bridged across for awhile by fine filaments. The two groups of fibres next undergo a gradual process of conversion into the daughter-nuclei (*e-h*).

It will be seen, from the above account, that the division of the *nucleus* of the cartilage cell resembles on the whole that which has been observed in other cells, The mode of division of the *cell-substance* is, however, different from that

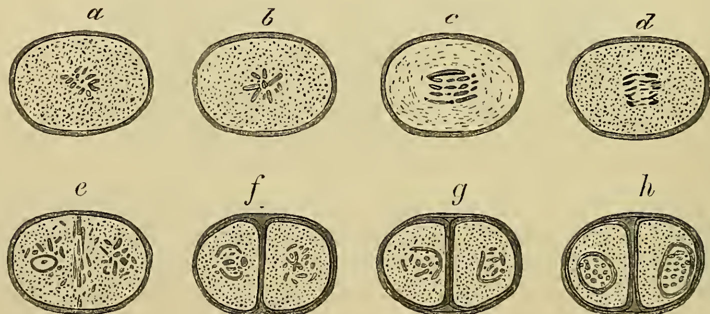


Fig. 294.—Division of a cartilage cell (Schleicher).

a-h, stages of division of a cell, as seen in the living cartilage of the salamander (the connection of the nucleoplasmic filaments could not be made out in the fresh condition). *a*, *b*, stellate phase ; *c*, *d*, commencing separation of the nucleo-plasmic filaments ; the further stages of separation are not represented ; *e*, filaments fully separated into two groups, and a septum beginning to be formed between them ; *f*, septum completed, seen to be double and continuous with capsules of daughter cells ; *g*, *h*, further stages in the formation of the daughter nuclei.

which obtains in most animal-cells, for in place of a constriction appearing and gradually separating the protoplasm into two halves from without in, a partition is formed (*e*), in the middle of the now elongated cell, as is most commonly the case in the division of plant-cells. The septum, as soon as it is broad enough, is seen to consist of two layers, which are continuous with the capsules of the two daughter-cells (*f*).

In the case of elastic cartilage the matrix is at first hyaline, and the elastic fibres are subsequently produced in it. They appear in the form of fine granules in those parts of the matrix that are in immediate contiguity with the cartilage-cells. In the cartilage of the external ear this change occurs about the fifth month of intra-uterine life, commencing in the more central parts, and gradually extending outwards towards the perichondrium.

The mode of development of white fibro-cartilage has not been fully ascertained, but it appears that the fibres are formed at the same time as the matrix instead of subsequently as in the case of elastic cartilage.

The vital changes which occur in cartilage take place very slowly. Its mode of nutrition has been already referred to ; it is subject to absorption, and when a portion is absorbed in disease or removed by the knife, it is regenerated very slowly. A wound in cartilage is usually at first healed by connective tissue, which becomes gradually transformed into hyaline cartilage. The reappearance of the latter seems, however, to depend upon the presence of the perichondrium, this membrane fulfilling, although perhaps not to so marked an extent, the same functions in the regeneration of cartilage as does the periosteum in the regeneration of bone. Schwalbe found that the cartilage of the rabbit's ear grew only by apposition at its margins and surfaces, and not interstitially ; but it is certain that the temporary cartilages grow in the manner last mentioned.

Probably the rib-cartilages grow in two ways, viz. : (1) by interstitial expansion accompanied by multiplication of the cells and increase of the matrix ; (2) by apposition, fresh cartilage being formed under the perichondrium by transformation of its fibrous tissue into cartilage (metaplastic formation).

When a cartilage is fractured, as sometimes happens with the rib-cartilages, the broken surfaces become connected, especially at their circumference, by fibrous or dense areolar tissue, and often by a bony clasp.

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BONE OR OSSEOUS TISSUE.

The bones are the principal organs of support, and the passive instruments of locomotion. Connected together in the skeleton, they form a framework of hard material, which affords attachment to the soft parts, maintains them in their due position, and shelters such as are of delicate structure, giving stability to the whole fabric, and preserving its shape ; and the different pieces of the skeleton being joined moveably together, serve also as levers for executing the movements of the body.

While substantially consisting of hard matter, bones in the living body are covered with periosteum and filled with marrow ; they are also pervaded by blood-vessels for their nutrition.

Bone has a white colour, with a pink and slightly bluish tint in the living body. Its hardness is well known, but it also possesses a certain degree of toughness and elasticity ; the last property is peculiarly well marked in the ribs. Its specific gravity is from 1.87 to 1.97.

Chemical Composition.—Bone consists of an earthy and an animal part, intimately combined together ; the former gives hardness and rigidity, the latter tenacity, to the osseous tissue.

The earthy part may be obtained separate by calcination. When bones are burned in an open fire, they first become quite black, like a piece of burnt wood, from the charring of their animal matter ; but if the fire be continued with free access of air, this matter is entirely consumed, and they are reduced to a white, brittle, chalk-like substance, still preserving their original shape, but with the loss of about a third of their weight. The earthy constituent, therefore, amounts to about two-thirds of the weight of the bone. It consists principally of phosphate of lime, with about a fifth part of carbonate of lime, and much smaller proportions of fluoride of calcium, chloride of sodium, and magnesian salts.

The animal constituent may be freed from the earthy, by steeping a bone in diluted hydrochloric acid. By this process the salts of lime are dissolved out, and a tough flexible substance remains, which, like the earthy part, retains the perfect figure of the original bone in its minutest details ; so that the two are evidently combined in the most intimate manner. The animal part is often named the cartilage of bone, but improperly, for it differs entirely from cartilage in structure, as well as in physical properties and chemical nature. It is much softer and much more flexible, and, by boiling, it is almost wholly resolved into gelatin. It may accordingly be extracted from bones, in form of a jelly, by boiling them for a considerable time, especially under high pressure.

The lining membranes of the Haversian canals and the walls of the lacunæ are formed of a material which resists the action of strong hydrochloric acid (which dissolves the remainder of the animal matter) (Langer).

In the compact substance of a femur that had been long buried. Aeby found only 16·5 per cent. of animal matter.

The fluoride of calcium is found in larger quantity in fossil than in recent bones.

MINUTE STRUCTURE OF BONE.

On sawing up a bone, it will be seen that it is in some parts dense and close in texture, appearing like ivory ; in others open and reticular ; and anatomists accordingly distinguish two forms of osseous tissue, viz., the *compact*, and the *spongy* or *cancellated*. On closer examination, however, especially with the aid of a magnifying glass, it will be found that the bony matter is everywhere porous in a greater

or less degree, and that the difference between the two varieties of tissue depends on the different amount of solid matter compared with the size and number of the open spaces in each ; the cavities being very small in the compact parts of the bone, with much dense matter between them ; whilst in the cancellated texture the spaces are large, and the intervening bony partitions thin and slender. There is, accordingly, no abrupt limit between the two,—they pass into one another by degrees, the cavities of the compact tissue widening out, and the reticulations of the cancellated

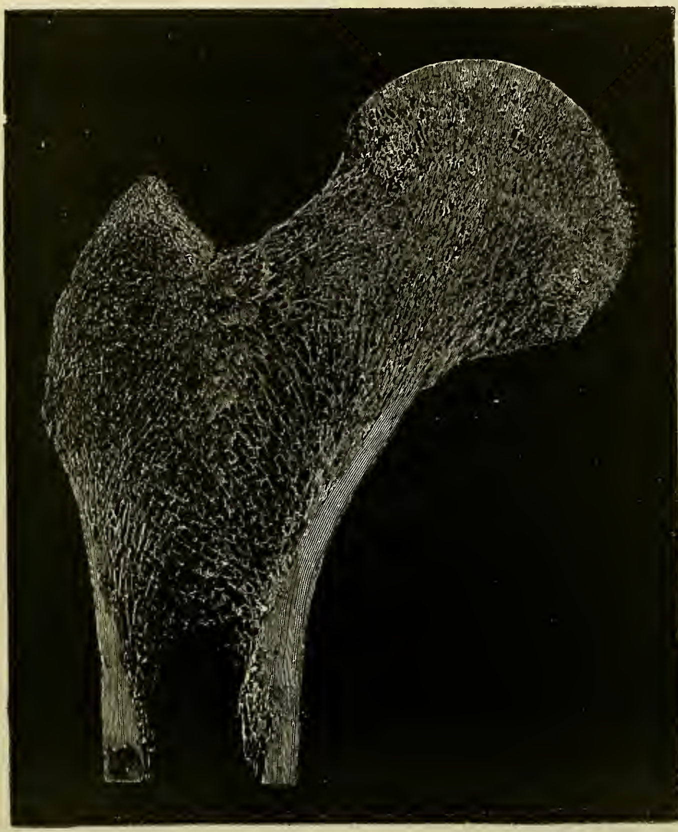


Fig. 295.—Longitudinal section through the upper end of the femur showing the cancellous structure of the head and the compact substance of the shaft. (From a photograph by Zaaijer.)

becoming closer as they approach the parts where the transition between the two takes place.

In all bones, the part next the surface consists of compact substance, which forms an outer shell or crust, whilst the spongy texture is contained within. In a long bone, the large round ends are made up of spongy tissue, with only a thin coating of compact substance (fig. 295) ; in the hollow shaft, on the other hand, the spongy texture is scanty, and the sides are chiefly formed of compact bone, which increases in thickness from the extremities towards the middle, at which point the girth of the bone is least, and the strain on it greatest. In tabular bones, such as those of the skull, the compact tissue forms two plates, or tables, as they are called, inclosing between them the spongy texture, which in such bones is usually named *diploë*. The short bones, like the ends of the long, are spongy throughout, save at their

surface, where there is a thin crust of compact substance. In the complex or mixed bones, such as the vertebræ, the two substances have the same general relation to each other ; but the relative amount of each in different parts, as well as their special arrangement in particular instances, is very various.

On close inspection the cancellated texture of bone is seen to be formed of slender bars or spicula and thin lamellæ, which meet together and join in a reticular manner, producing an open structure which has been compared to lattice-work (*cancelli*), and hence the name usually applied to it. In this way considerable strength is attained without undue weight, and it may usually be observed that the

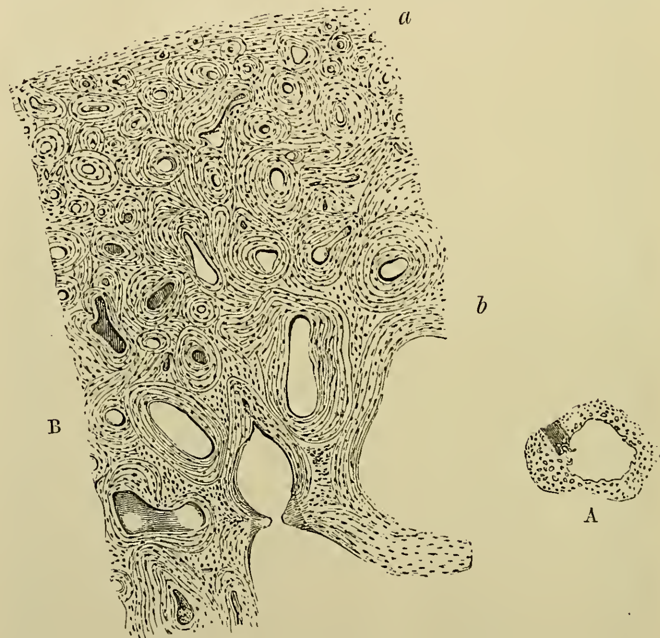


Fig. 296.—A, Transverse section of a bone (ulna) deprived of its earth by acid (Sharpey).

The openings of the Haversian canals are seen. Natural size. A small portion is shaded to indicate the part magnified in Fig. B.

B, Part of the Section A, magnified 20 diameters.

The lines indicating the concentric lamellæ are seen, and among them the lacunæ appear as little dark specks.

strongest laminæ run through the structure in those directions in which the bone has naturally to sustain the greatest pressure. The open spaces or areolæ of the bony network communicate freely together ; in the fresh state they contain marrow and blood-vessels.

Haversian canals.—The compact tissue is also full of holes; these, which are very small, are best seen by breaking across the shaft of a long bone near its middle and examining it with a common magnifying glass. Numerous little round apertures (fig. 296 A) may then be seen on the broken surface, which are the openings of short longitudinal passages running in the compact substance, and named the *Haversian canals*, after Clopton Havers, an English physician and writer of the seventeenth century, who more especially called attention to them. Blood-vessels run in these canals, and the widest of them also contain marrow. They are from $\frac{1}{1000}$th to $\frac{1}{200}$th of an inch in diameter : there are some no more than $\frac{1}{2000}$th, but these are

rare; the medium size is about $\frac{1}{500}$th. The widest are met with nearest the medullary cavity, and the narrower towards the circumference of the bone. They are quite short, as may be seen in a longitudinal section, oblique communications connecting them freely both longitudinally and laterally. Those which are next the circumference of the bone, open by minute pores on its external surface, and the innermost ones open widely into the medullary cavity; so that these short channels collectively form a sort of irregular network of tubes running through the compact tissue, in which the vessels of that tissue are lodged, and through the medium of which these vessels communicate together, not only along the length of the bone but from its surface to the interior through the thickness of the shaft. The canals of the compact tissue in the other classes of bones have the same general characters, and for the most part run parallel to the surface.

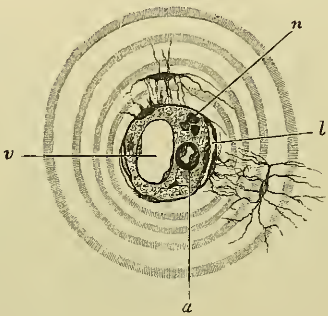


Fig. 297.—Section of a Haversian canal, showing its contents. Highly magnified. (E. A. S.)

a, small arterial capillary vessel; *v*, large venous capillary; *n*, pale nerve-fibres cut across: *l*, cleft-like lymphatic vessel: one of the cells forming its wall communicates by fine branches with the branches of a bone-corpuscle. The substance in which the vessels run is connective tissue with ramified cells; its finely granular appearance is probably due to the cross section of fine fibrils.

Most of the Haversian canals contain two small blood-vessels, arterial and venous (fig. 297), together with a small amount of delicate connective tissue containing branched cells, which are flattened close to the bone, and communicate by their branches with the ramifications of corpuscles in the substance of the bone.

Lamellæ.—On viewing a thin transverse section of a long bone with a microscope of moderate power, especially after the earthy part has been removed by acid (fig. 296 B; fig. 297), the opening of each Haversian canal appears to be surrounded by a series of concentric rings. This appearance is occasioned by the transverse sections of concentric *lamellæ* which surround the canals. The rings are not all complete, for here and there one may be seen ending between two others. In some of the sets, the rings are nearly circular, in others oval,—differences which seem mostly to depend on the direction in which the canal happens to be cut: the aperture too, may be in the centre or more or less to one side, and in the latter case the rings are usually narrower and closer together on the side towards which the aperture deviates. Again, some of the apertures are much lengthened or angular in shape, and the lamellæ surrounding them have a corresponding disposition. Besides the lamellæ surrounding the Haversian canals, there are others disposed conformably with the circumference of the bone (fig. 296 B, *a*); most of these are near the surface, but others run between the Haversian sets, by which they are interrupted in many places (fig. 303). Lastly, in various parts of the section, lines are seen which indicate lamellæ, differing in direction from both of the above-mentioned orders.

The appearance in a longitudinal section of the bone is in harmony with the account above given: the sections of the lamellæ are seen as straight and parallel lines, running in the longitudinal direction of the bone, except when the section happens to have passed directly or slantingly across a canal: for wherever this occurs there is seen, as in a transverse section, a series of rings, generally oval and much lengthened on account of the obliquity of the section.

Many of the Haversian canals which pass through the circumferential or periosteal lamellæ carrying blood-vessels from the periosteum into the bone, are not surrounded by concentric

lamellæ, but are mere channels piercing the periosteal lamellæ. They are often spoken of as Volkmann's canals.

The cancellated texture has essentially the same lamellar structure. The slender bony walls of its little cavities or areolæ are made up of superimposed lamellæ, like those of the Haversian canals, only they have fewer lamellæ in proportion to the width of the cavities which they surround ; and, indeed, the relative amount of solid matter and open space constitutes, as already said, the only difference between the two forms of bony tissue : the intimate structure of the solid substance and the manner of its disposition round the cavities being essentially the same in both.

Lacunæ and canaliculi.—All over the section numerous little dark specks are seen among the lamellæ. These were named the "osseous corpuscles ;" but as it is now known that they are in reality minute cavities existing in the bony substance, the name of *lacunæ* has since been more fittingly applied to them. To see the lacunæ

Fig. 298.—Transverse section of compact tissue (of humerus), magnified about 150 diameters (Sharpey).

Three of the Haversian canals are seen, with their concentric rings ; also the lacunæ, with the canaliculi extending from them across the direction of the lamellæ. The Haversian apertures had become filled with air and débris (from the grinding), and therefore appear black in the figure, which represents the object as viewed with transmitted light.

properly, however, sections of unsoftened bones must be prepared and ground very thin, and a magnifying power of from 200 to 300 must be employed. Such a section, viewed with transmitted light, has the appearance represented in fig. 298. The openings of the Haversian canals are seen with their encircling lamellæ, and among these the lacunæ, which are mostly ranged in a corresponding order, appear as black, opaque or nearly opaque oblong spots, with fine dark lines extending from them and causing them to look not unlike little black insects. The dark appearance is due to the fact that the little cavities have become filled with air in the dry bone, and when the same section is seen against a dark ground, with the light falling on it (as we usually view an opaque object), the little bodies and lines appear quite white, like figures drawn with chalk on a slate, and the intermediate substance, being transparent, now appears dark.

The lacunæ, as already stated, are minute recesses in the bone, and the lines extending from them are fine pores or tubes named *canaliculi*, which issue from their

cavity. The lacunæ present some variety of figure, but in such a section as that represented they for the most part appear irregularly fusiform, and lie nearly in the same direction as the lamellæ between which they are situated; or, to speak more correctly, they are flattened and extended conformably with the lamellæ; for when the bone is cut longitudinally, their sections still appear fusiform and are still more lengthened out in the direction of the lamellæ. The canaliculi, on the other hand, pass across the lamellæ, and they communicate with those proceeding from the next range of lacunæ, so as to connect the little cavities with each other; and thus since the canaliculi of the most central range open into the Haversian canal, a system of continuous passages is established by these minute tubes and their lacunæ, along which fluids may be conducted from the Haversian canal through its series of surrounding lamellæ; indeed, it seems probable that a chief purpose of these minute passages is to allow nutrient matter to be conveyed from the vascular Haversian canals through the mass of hard bone which lies around and between them. In like manner the canaliculi open into the great medullary canal, and into the cavities of the cancellated texture; for in the thin bony parietes of these cavities lacunæ are also contained; they exist, indeed, in all parts of the bony tissue. The canaliculi which radiate outwards from the lacunæ near the periphery of the Haversian systems do not as a rule communicate with those of the neighbouring Haversian system, but bend round and are joined to one another.

Cells of bone.—As first shown by Virchow, each lacuna is occupied by a flattened nucleated cell, which sends branches along the canaliculi; and later observers (Rouget, Neuman,) have been able to detach the proper wall of the lacuna

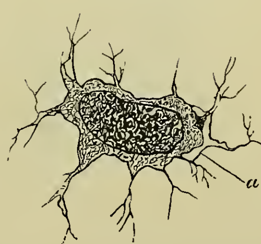


Fig. 299.—A BONE-CELL ISOLATED AND HIGHLY MAGNIFIED (after Joseph).

a, proper wall of the lacuna, shown at a part where the corpuscle has shrunk away from it.

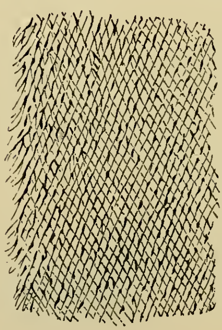
and its appertaining canaliculi after decalcification, and to obtain it separate with its included corpuscle (fig. 299). It can scarcely be doubted that the protoplasm of the nucleated corpuscle takes an important share in the nutritive process in bone, and very probably serves both to modify the nutritive fluid supplied from the blood and to further its distribution through the lacunar and canalicular system of the bony tissue. Virchow showed that the corpuscles of bone are homologous with those of ordinary connective tissue: to this it may be added that the enclosing lacunæ and canaliculi are to be looked upon as corresponding to the cell-spaces of that tissue.

Apertures and decussating fibres of the lamellæ.—With a little pains thin films may be peeled off in a longitudinal direction from a piece of bone that has been softened in acid. These for the most part consist of several lamellæ, as may be seen at the edge, where the different layers are usually torn unequally, and some extend farther than others. Examined in this way, under the microscope, the lamellæ are seen to be perforated with fine apertures placed at very short distances apart. These apertures were described by Deutsch[1]; they appear to be the transverse sections of the canaliculi already described, and their relative distance and position accord sufficiently with this explanation. According to this view, therefore, the canaliculi might (in a certain sense) be conceived to result from the apposition of a series of perforated plates, the apertures of each plate corresponding to those of the plates contiguous with it; or they might be compared to holes bored to some

[1] De Penitiori Ossium Structurâ. Wratisl. 1834, p. 17, Fig. 6.

depth in a straight or crooked direction through the leaves of a book, in which case it is plain that the perforations of the adjoining leaves would correspond ; it being understood, however, that the passages thus formed are most likely bounded by proper parietes. The apertures now referred to must be distinguished from larger holes seen in some lamellæ, which give passage to the perforating fibres to be mentioned further on.

But the lamellæ have a further structure. To see this, the thinnest part of a detached shred or film must be examined, as shown in figs. 300 and 302 ; it will then appear plainly that they are largely made up of transparent fibres, decussating with each other in the form of an exceedingly fine network. In the Haversian systems these decussating fibres cross one another in different lamellæ at right angles (v. Ebner), but in most other situations at more or less acute angles, and they are united here and there by obliquely passing fibres, so that they cannot be teased out from one another ; but at the torn edge of the lamella they may often be seen separate for a little way, standing out like the threads of a fringe. Most generally they are straight, as represented in fig. 300 ; but they are not always so ; for in some parts they assume a curvilinear direction (fig. 302). Acetic or hydro-



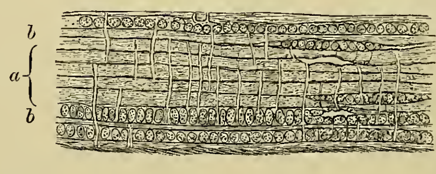


Fig. 300.—Thin layer peeled off from a softened bone, as it appears under a magnifying power of 400 diameters (Sharpey).

This figure, which is intended to represent the reticular structure of a lamella, gives a better idea of the object when held rather farther off than usual from the eye.

Fig. 301.—Small part of a longitudinal section of decalcified tibia. Highly magnified (after v. Ebner).

a, series of six lamellæ which are cut for the most part in the direction of the fibrils, so that they appear longitudinally striated ; *b*, *b*, lamellæ, the fibrils of which are cut across ; the arrangement of the fibrils into bundles is indicated. Two lacunæ are seen lying between the lamellæ, also canaliculi piercing the lamellæ.

chloric acid causes these fibres to swell up and become indistinct, like the white fibres of connective tissue ; care must therefore be taken in their examination that the remains of the decalcifying acid be removed from the tissue, by maceration in water or in solutions of neutral salts. Moreover, the fibro-reticular structure is not equally distinct in all parts ; for in some places it is less decidedly marked, as if the fibrillation were incompletely developed.

The decussating fibres which constitute the lamellæ were discovered by Sharpey, and their constant presence was taught by him for a long time before they were admitted by other histologists. It has lately been shown by v. Ebner that the decussating fibres of Sharpey are in reality themselves composed of exquisitely fine fibrils, so that they correspond with bundles of white connective tissue fibres rather than with single fibres. Like the connective tissue fibrils these of the bone are doubly refracting, and they are said (Ebner) not to be calcified.

the deposit of calcareous matter being confined to the matrix in which they are embedded. They appear to be united into the lamellæ by a matrix or ground-substance, and take different directions in successive lamellæ, so as to produce a granular or a striated appearance according as they happen to be cut transversely or longitudinally (fig. 301).

In thin sections of bone, the concentric lines or rather bands which represent the cut edges of the lamellæ show the section of the decussating fibres as round or angular dots, themselves punctated, which lie embedded in the homogeneous ground-substance (fig. 301, *b*). The lamellæ are separated from one another by the lacunæ which lie between them, where these are absent they are joined together by the ground-substance; they are also united by occasional bundles of fibres passing obliquely from one lamella to the other.

Perforating fibres.—It was further shown by Sharpey that in many instances the lamellæ are perforated by fibres, which pass through them in a perpendicular or oblique direction, and, as it were, bolt them together. These perforating fibres may be seen, with the aid of the microscope, in a thin transverse slice of a decalcified cylindrical or cranial bone, on pulling asunder the sections of the lamellæ (as in fig. 304). In this way some lamellæ will generally be observed with fibrous pro-

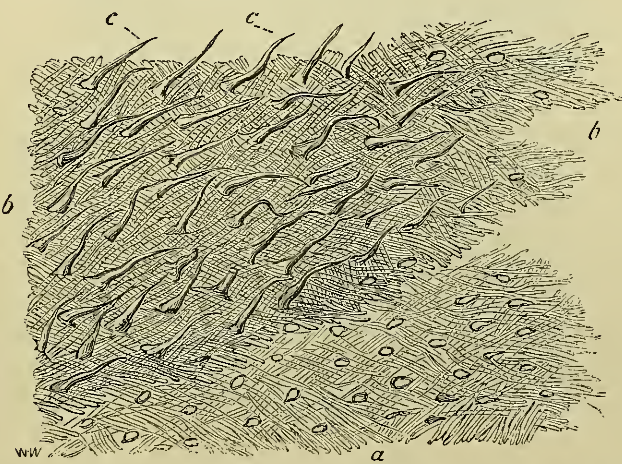


Fig. 302.—Lamellæ torn off from a decalcified human parietal bone at some depth from the surface (Sharpey).

a, lamellæ, showing decussating fibres; *b*, *b*, thicker part, where several lamellæ are superposed; *c*, *c*, perforating fibres. Apertures through which perforating fibres had passed, are seen especially in the lower part, *a*, *a*, of the figure. Magnitude as seen under a power of 200, but not drawn to a scale (from a drawing by Allen Thomson).

cesses attached to them (fig. 304, *b*) of various lengths, and usually tapering and pointed at their free extremities, but sometimes truncated—probably from having been divided by the knife. These fibres have obviously been drawn out from the adjacent lamellæ, through several of which they must have penetrated. Sometimes, indeed, indications of perforations may be recognized in the part of the section of bone from which the fibres have been pulled out (fig. 304, *c*). The processes in question are thus, so to speak, viewed in profile; but they may frequently also be seen on the flat surface of detached lamellæ (fig. 302), projecting like nails driven perpendicularly.

The perforating fibres are, like the decussating fibres, for the most part bundles of fibrils which agree in character with those of the white fibrous tissue; but some, as shown by H. Müller, are of the nature of elastic tissue (fig. 303, *e*). In some parts they escape calcification, and thus, as they shrink in drying, leave tubes or channels in the dry bone, generally leading from the surface inwardly; but these

uncalcified fibres are by no means frequent (Sharpey). The perforating fibres are often connected with the periosteum, as is the case with most of those which penetrate the external table of the cranial bones; but in cross sections of cylindrical bones they often appear to spring with their broad ends from the deeper lamellæ (with the fibres of which they may be directly continuous), and especially from those near the circumference of a Haversian system, and taper outwards into fine points, which do not reach the periosteum (fig. 303), although without doubt they must, like the bony layers in which they occur, have been formed by subperiosteal ossification. They are never found in the concentric systems of Haversian

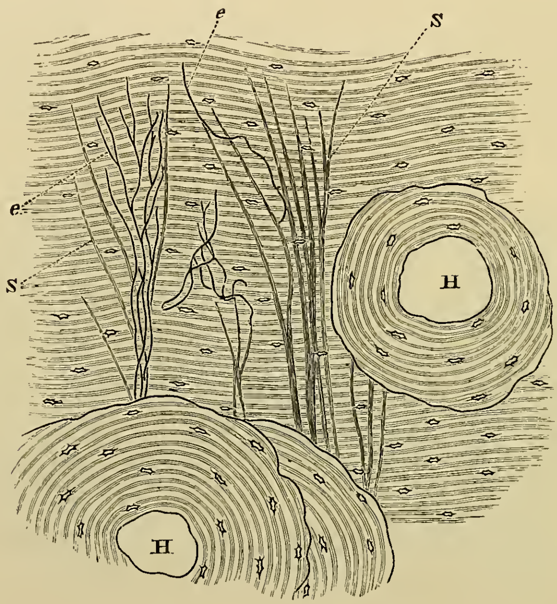


Fig. 303.—Transverse section of decalcified human tibia, from near the surface of the shaft (E. A. S.).

H, H, Haversian canals, with their systems of concentric lamellæ; in all the rest of the figure the lamellæ are circumferential.

s, ordinary perforating fibres of Sharpey; *e*, *e*, elastic perforating fibres. Drawn under a power of about 150 diameters.

lamellæ. Perforating fibres exist abundantly in the *crusta petrosa* of the teeth (Sharpey).

Where tendons or ligaments are inserted into bone, the fibre-bundles of the tendon are continued into the bone as perforating fibres, so that the attachment of tendon to bone is thus rendered very intimate. Some of the bundles of white fibres of the periosteum may also, as above mentioned, pass into the bone as perforating fibres, and the same is the case with the elastic fibres.

The animal basis of bone is made up essentially, as we have seen, of lamellæ composed of fine decussating or reticular fibril-bundles embedded in a ground-substance; but interposed among these lamellæ, layers are here and there met with of a different character, having a granular aspect, with the lacunæ very conspicuous and regularly arranged, and sometimes appearing as if surrounded by faintly defined areolæ. These generally incomplete layers are often bounded by a scalloped border, as if made up of confluent round or oval bodies; this is indicated also by the occa-

sional occurrence of oval or flattened spheroidal bodies singly or in small groups near the border of the layers, each with a lacuna in the centre (fig. 305). In some parts the granular substance is obscurely fibrous, and transitions may be observed to the

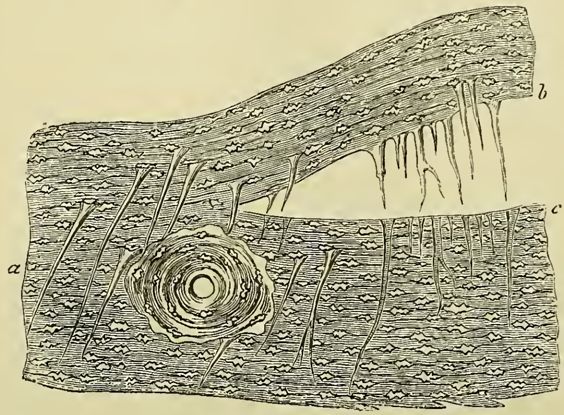


Fig. 304.—Magnified view of a perpendicular section through the external table of a human parietal bone, decalcified (H. Müller).

At *a*, perforating fibres in their natural situation; at *b*, others drawn out by separation of the lamellæ; at *c*, the holes or sockets out of which they have been drawn (H. Müller).

well-marked reticular laminæ. The layers described appear principally to occur near the surface of the compact tissue, and at the circumference of many of the systems of concentric Haversian lamellæ.

Irregular layers of rounded bodies, apparently solid and without central cavity, are also sometimes seen, and are well represented in figure 306. These layers are

Fig. 305.—Small part of a section through the shaft of a femur (human, 16 years) taken a short distance from the epiphysis. 230 diameters. (Kölliker.)

a, remains of calcified cartilage; *b*, bony deposit in Howship's foveolæ (absorption spaces); *c*, subsequent deposit of lamellar bone.

met with chiefly near the surface of the shaft of long bones, lying among the circumferential laminæ, and apparently forming only part of a circuit. They can occasionally be recognised in a transverse section as short curvilinear bands of peculiar aspect, broader in the middle and thinning away at the ends, appearing here and there between the cut edges of two ordinary circumferential laminæ.

Finally, spaces are occasionally seen in a section of bone, which are characterized by an eroded outline, but in some cases they may be partially filled up by concentric

lamellæ. These were named "Haversian spaces" by Tomes and de Morgan, and they are interpolated or intruded amongst the regular Haversian systems, some of which may have been cut in upon in the excavation of the space. It was further noticed by Tomes and de Morgan that the spaces in question may sometimes be seen being filled up at one part by the deposition of lamellæ, whilst they are extending themselves by absorption at another. The Haversian spaces are most numerous in young and growing bones, but they occur also after growth is completed.

The three appearances above mentioned are due to the peculiar manner in which the absorption of bone occurs; for it is effected, as will presently be described, by

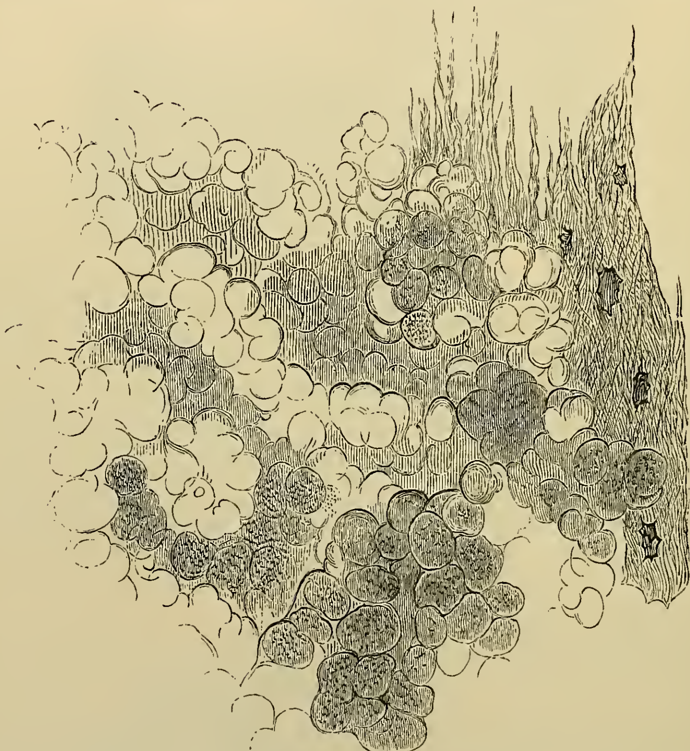


Fig. 306.—Portion of a nodulated layer of bone-tissue from near the surface of the shaft of a decalcified humerus (Sharpey).

At one side shreds of fibrous lamellæ are seen in the figure. Magnified 300 diameters. From a drawing by Allen Thomson.

the agency of large multinucleated cells, which excavate little hemispherical pits (foveolæ of Howship) in the osseous tissue. If the process of absorption should cease and should be succeeded by a re-deposition of osseous substance, the new osseous matter filling up the hollows of the absorbed surface exhibits, when it is detached, a raised impression corresponding with the hollows into which it fitted.

In young bones the lamellar character is far less distinct than in adult bones, the tissue being constituted chiefly of bundles of fibres which interlace in every direction in the ground-substance; in this reticular form of osseous tissue the lacunæ are both more numerous and irregular than in lamellated bone.

When tendons become ossified, as is often the case, especially in birds, little but a calcification of the ground-substance of the tendon occurs, so that, after decalcifying, the tendinous structure again becomes manifest.

The exact knowledge we possess of the minute structure of osseous tissue is largely the result of the careful investigation of the late Professor Sharpey, whose account, published in the fifth edition of this work in 1845, has needed no erasure, and but little addition, even to the present day. His labours in this field have been to a certain extent recognized in the adoption of the name "fibres of Sharpey" for the perforating fibres discovered by him, but it is only of late that the facts which he demonstrated are becoming understood and their significance appreciated by histologists.

THE PERIOSTEUM.

The **periosteum**, as already stated, is a fibrous membrane which covers the bones externally. It adheres to them very firmly, and invests every part of their surface, except where they are covered with cartilage.

It is composed of two layers; the outer, consisting chiefly of white fibres, and containing occasional fat-cells, is the means of supporting numerous blood-vessels destined for the bone, which ramify in the membrane, and at length send their minute branches into the Haversian canals of the compact substance, accompanied by processes of filamentous tissue derived from, or at least continuous with, the periosteum. The inner layer is largely made up of elastic fibres, frequently in several distinct strata. Between it, however, and the proper osseous tissue there is a fibrous stratum containing in the young bone a number of granular corpuscles (osteoblasts), while in the adult bone these have become flattened out into an epithelioid layer covering the osseous substance, and are in many places separated by a cleft-like space (serving probably for the passage of lymph) from the rest of the periosteum (Schwalbe).

By treating the membrane with nitrate of silver, lymphatics are discovered in it accompanying the blood-vessels in the outer layer; and, as in other aponeurotic structures, extensive epithelioid markings, covering a great part of the surface, are brought into view.

Fine nerves spread out in the periosteum; they are chiefly associated with the arteries, and for the most part destined for the subjacent bone; but some are for the membrane itself, and some of these end in Pacinian corpuscles.

The chief use of the periosteum is to support the vessels going to the bone, and afford them a bed in which they may subdivide into fine branches, and so enter the dense tissue at numerous points. Hence, when the periosteum is stripped off at any part, there is great risk that the denuded portion of the bone will die and exfoliate. The periosteum also contributes to give firmer hold to the tendons and ligaments where they are fixed to bones. Its relation to the growth and renewal of bone will be referred to later on.

THE MARROW.

The **marrow** (*medulla ossium*) is lodged in the interior of the bones; it fills up the hollow shaft of long bones and occupies the cavities of the cancellated structure; it extends also into the Haversian canals—at least into the larger ones—along with the vessels. A fine layer of a highly vascular areolar tissue lines the medullary canal, as well as the smaller cavities which contain marrow; this has been named the medullary membrane, internal periosteum, or *endosteum;* but it cannot be detached as a continuous membrane. Its vessels join on the one side those of the osseous substance, and on the other side are continuous with the capillaries of the marrow.

The marrow differs considerably in different situations. Within the shaft of the

long bones in man it is of the character of ordinary adipose tissue, but the fat-cells are supported by a kind of retiform tissue, and between them elements occur similar to those immediately to be mentioned in the red marrow. In short bones, and in the cancellated ends of long bones, but especially in the cranial diploë, the bodies of the vertebræ, the sternum, and the ribs, the marrow is red or reddish in colour, of more fluid consistence, and with very few fat-cells. While, however, the fat-cells are scanty in the red-coloured marrow, it contains numerous round leucocytes —the proper *marrow-cells* of Kölliker (fig. 307, *e—i*). These in general appearance resemble the pale corpuscles of the blood, but are larger, with a clearer protoplasm and a relatively larger nucleus. Like the pale corpuscles, they exhibit amœboid movements. Amongst them are smaller cells which have a reddish colour, and resemble in appearance the primitive nucleated corpuscles of the embryo (fig. 307, *j—t*); these are the cells (erythroblasts) which are concerned in the formation of the red blood-disks, and according to some authors are themselves

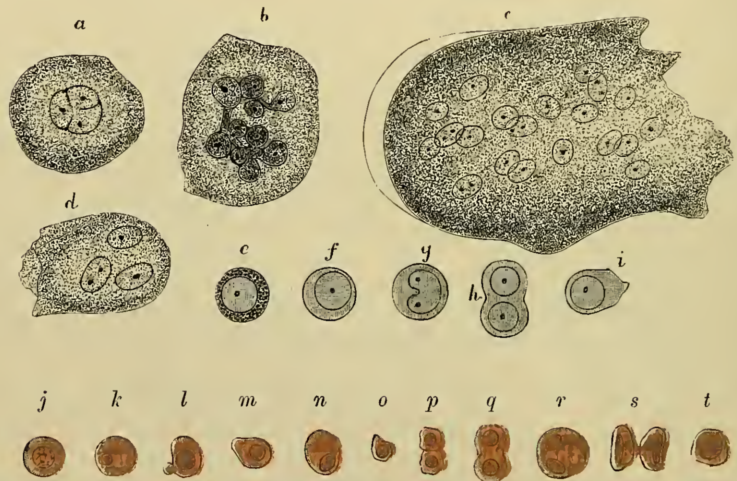


Fig. 307.—Cells of the red marrow of the guinea-pig. Highly magnified. (E. A. S.)

a, a large cell the nucleus of which appears to be partly divided into three by constrictions; *b*, a cell the enlarged nucleus of which shows an appearance of budding into a number of smaller nuclei; *c*, a so-called giant-cell or myeloplaxe with many nuclei; *d*, a smaller myeloplaxe with three nuclei; *e—i*, proper cells of the marrow; *j—t*, various forms of coloured nucleated cells, some undergoing division.

derived from colourless marrow-cells or from pale blood-corpuscles (p. 219). It is, however, doubtful if this is so; it is more probable that they are the direct descendants of the nucleated red corpuscles of the early embryo. Like these they are amœboid and divide by karyokinesis. They appear to be formed into blood-disks by the disappearance of the nucleus and the moulding of the cell protoplasm into the biconcave discoid shape. It is probably by virtue of their amœboid properties that they pass into the venous capillaries of the marrow, but some may be contained within the vessels, and in birds all the erythroblasts are found within the lumen of the venous capillaries (Bizzozero and Torre).

Cells have occasionally been noticed containing one or more red corpuscles in their interior (Osler): whether these have been developed *in situ* in a manner similar to that previously described in connective tissue corpuscles of the young animal, or have been taken into the interior of an amœboid cell, there to be transformed into pigment-granules, is not certainly known. Cells containing reddish pigment-

granules are, however, not uncommon. There further occur in the marrow, especially in the neighbourhood of the osseous substance, large multi-nucleated protoplasmic masses (*myeloplaxes* of Robin, fig. 307, *a—d*), which, as pointed out by Kölliker, appear to be more especially concerned with the process of absorption of bone, under which head they will subsequently be further alluded to. The myeloplaxes vary much in size, but are always larger than the proper marrow-cells. Their nucleus is not always multiple, but when single it is usually enlarged, and presents indications of division (fig. 307, *a*) ; it may even be so constricted as to exhibit an irregularly moniliform appearance (fig. 307, *b*).

Blood-vessels.—The bones are well supplied with blood-vessels. A network of periosteal vessels covers their outer surface ; fine vessels run from this through all parts of the compact tissue in the Haversian canals ; others penetrate to the cavities of the spongy part, in which they ramify ; and a considerable artery goes to the marrow in the central part of the bone. In the long bones this *medullary artery*, often, but improperly, called "the nutritious artery," passes into the medullary canal, near the middle of the shaft, by a hole running obliquely through the compact substance. The vessel, which is accompanied by one or two veins, then sends branches upwards and downwards in the middle of the marrow ; from these branches arterial capillaries pass radially towards the periphery. The comparatively narrow arterial capillaries pass suddenly at the periphery of the marrow into the wide venous ones, which form a close network of large thin-walled vessels throughout the medullary tissue, so that the current of blood must be considerably retarded both in these and in the large thin-walled veins.

The ramifications of the medullary artery anastomose with the arteries of the compact and cancellated structure ; indeed, there is a free communication between the finest branches of all the vessels which proceed to the bone, and there is no strictly defined limit between the parts supplied by each. In the thigh bone there are frequently two medullary arteries entering at different points.

The veins of the cancellated texture are peculiar and deserve special notice. Their arrangement is best known in the bones of the skull, where, being lodged in the diplöe or spongy texture between the outer and inner compact tables, they have received the name of the diplöic veins. They are large and numerous, and run separately from the arteries in canals formed in the cancellated structure, the sides of which are constructed of a thin lamella of bone, perforated here and there for the admission of branches from the adjoining cancelli. Being thus inclosed and supported by the hard structure, the veins have exceedingly thin coats. They issue from the bone by special apertures of large size. A similar arrangement is seen in the bodies of the vertebræ, whence the veins come out by large openings on the posterior surface. In the long bones numerous apertures may be seen at the ends, near the articular surfaces ; some of these give passage to arteries, but the greater number, as well as the larger of them, are for the veins of the cancellated texture, which run separately from the arteries.

According to Hoyer and Rindfleisch the venous capillaries and veins of the red marrow have incomplete walls, or rather are channels bounded only by the medullary parenchyma, so that the blood-corpuscles which are being formed from marrow-cells can readily get into the circulation. Langer, on the other hand, found the vascular system of the marrow to be a closed one. In birds, this is certainly the case according to the testimony of Bizzozero and of Denys, but in mammals it is doubtful if the vascular walls are everywhere complete.

The blood coming from the marrow possesses a large number of pale corpuscles, and sometimes nucleated red corpuscles can be detected in it.

Lymphatics.—In addition to the lymphatics in the periosteum (which have already been mentioned), there are others in the Haversian canals accompanying the

vessels (fig. 297, *l*), and often partially or wholly enclosing them (perivascular). The lymph or plasma of the blood is enabled to penetrate the hard bony substance by means of the lacunæ and communicating canaliculi, which appear to bear the same relation to the lymphatics as do the cell-spaces of ordinary connective tissue to the lymphatics of that tissue.

The fine **nerves** which may be seen entering the bones along with the arteries are probably chiefly destined for those vessels ; it is not known whether any end in the bony tissue itself.

As far as can be judged from observations on man and experiments on the lower animals, the bones, as well as their investing periosteum, are scarcely if at all sensible in the healthy condition, although they are painfully so when inflamed.

FORMATION AND GROWTH OF BONE.

The foundation of the skeleton is laid at a very early period ; for, among the parts that appear soonest in the embryo, we distinguish the rudiments of the vertebræ and base of the skull, which afterwards form the great median column to which the other parts of the bony fabric are appended. But it is by their outward form and situation only, that the parts representing the future bones are then to be recognised ; for at that early period they do not differ materially in substance from the other structures of the embryo, being made up of mesoblastic cells, with a small amount of intercellular substance. Very soon, however, they become cartilaginous, and ossification in due time beginning in the cartilage and continuing to spread from one or from several points, the bony tissue becomes gradually formed.

But, while it is true with respect to the bones generally that their ossification commences in cartilage, it is not so in every instance. The tabular bones forming the roof of the skull may be adduced as a decided example to the contrary ; in these the ossification goes on in connective tissue altogether unconnected with any cartilage ; and even in the long bones, in which ossification undoubtedly commences and to a certain extent proceeds in cartilage, it will be afterwards shown that there is much less of the increment of the bone really owing to that mode of ossification than was at one time generally believed. It is necessary, therefore, to distinguish two species or modes of ossification, which for the sake of brevity may be called the *intramembranous* and the *intracartilaginous*.

INTRAMEMBRANOUS OSSIFICATION: OSSIFICATION IN CONNECTIVE TISSUE.

The tabular bones of the cranium, as already said, afford an example of this mode of ossification. The base of the skull in the embryo is cartilaginous ; but in the roof, that is to say, the part comprehending the parietal, the frontal, and a certain portion of the occipital bones, we find (except where there happen to be commencing muscular fibres) only the integuments, the dura mater, and an intermediate layer, in which the ossification proceeds.

The commencing ossification of the parietal bone, which may be selected as an example, appears to the naked eye in the form of a network in which the little bars or spicula of bone run in various directions, and meet each other at short distances. By-and-by the ossified part, becoming extended, gets thicker and closer in texture, especially towards the centre, and the larger bony spicula which now appear, run out in radiating lines to the circumference. The ossification continues thus to spread and consolidate until the parietal meets the neighbouring bones, with which it is at length united by sutures.

Fig. 308 represents the parietal bone of an embryo sheep about two inches and a half long, and shows the character of the ossification as it appears when the object

is magnified about twelve diameters. The bone is formed in membrane as in the human fœtus, but a thin plate of cartilage rises up on its inside from the base of the skull. The ossification, however, is decidedly unconnected with the cartilage, and goes on in a membrane lying outside of it.

When further examined with a higher magnifying power, the tissue or membrane in which the ossification is proceeding, appears to be made up of fibres and granular corpuscles, with a ground-substance between, and, in point of structure, may not unaptly be compared to connective tissue in a certain stage of development. The corpuscles are large and angular, and they are densely packed all over the area of ossification, covering the bony spicula, and filling up their interstices.

On observing more closely the points of the growing osseous rays at the circumference of the bone, where they shoot out into the soft tissue, it will be seen that the portion of them already calcified is granular and rather dark in appearance (fig. 309), but that this character is gradually lost as they are traced further outwards in the membrane, in which they are prolonged for a little way in form of soft and pliant bundles of transparent fibres (fig. 309, B, *of*).

Fig. 308.—Parietal bone of an embryo sheep. Size of the embryo 2½ inches. (Sharpey.)

The small upper figure represents the bone of the natural size, the larger figure is magnified about 12 diameters. The curved line, *a*, *b*, marks the height to which the subjacent cartilaginous lamella extended. A few insulated particles of bone are seen near the circumference, an appearance which is quite common at this stage.

These are termed *osteogenic fibres*, the soft transparent matter of which they are composed being known as osteogenic substance, or simply as *osteogen*. They exhibit faint fibrillation, and have been compared to bundles of white connective tissue fibres, with which, in some situations, they appear to be continuous (Gegenbaur). But although similar in chemical composition, they are somewhat different from these in appearance, having a stiffer aspect and straighter course, besides being less distinctly fibrillated. The fibres become calcified by the deposition within them of earthy salts in the form of minute globules, which produce a darkish granular opacity, until the interstices between the globules also become calcified, and the minute globules becoming thus fused together, the new bone again looks comparatively clear (fig. 309, B, *b*).

As already stated the fibrils which compose the osteogenic fibres themselves, are, according to v. Ebner, not calcified, but the calcification affects only the matrix which unites them.

The bundles of osteogenic fibres which prolong the bony spicules, generally spread out from the end of each spicule so as to come in contact with those from adjacent spicules. When this happens, the innermost or proximal fibres frequently grow together (fig. 309, B, *c*), whilst the other fibres partially intercross as they grow further into the membrane. The ossific process extends into the osteogenic

fibres *pari passu* with their growth, and thus new bony spicules become continually formed by calcification of the groups or bundles of osteogenic fibres.

The earthy deposit occasionally appears in an isolated patch here and there on some of the osteogenic fibres in advance of the main area of ossification (see fig. 309, A, *a*).

The osteogenic fibres become comparatively indistinct as they and the substance between them calcifies; they appear, however, to persist in the form of fine fibres, such as are seen in the lamellæ of the adult bone, although in the embryonic bone their disposition is not lamellated, the bony matter having a somewhat coarsely reticular structure.

In this way the first bony matter becomes formed as a perforated plate or network of osseous spicules, which, whilst becoming extended peripherally in the way above described, gradually becomes thicker nearer the centre, partly by the deposit of bony matter upon its surfaces, partly by the projection from them of bony spicules which are prolonged like those at the periphery by similar systems of osteogenic fibres. The perforations in these first-formed bony plates correspond to the bays which were seen between the advancing spicules, and to the meshes of the bony network formed afterwards by the junction of the spicules, and as the bone thickens they become enclosed and converted into reticulating interstices (like the canals of a sponge), which are occupied by blood-vessels, and by the corpuscles above mentioned. These corpuscles also everywhere cover the osteogenic fibres, to which their flattened sides are often applied (fig. 309, B, *ost*). Where the osteogenic fibres diverge from one another, the intervals are occupied by the same cells. It is probable that the osteogenic substance is formed by the agency of the cells in question, hence the name "osteoblasts" was assigned to them by Gegenbaur.

A

B

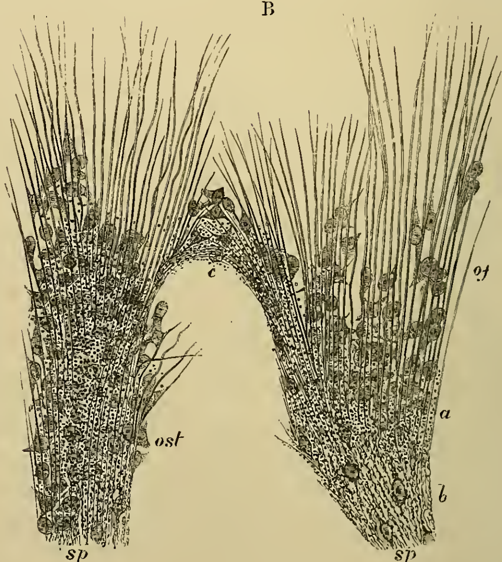


Fig. 309.—Part of the developing parietal bone of a fœtal cat ($1\frac{1}{2}$ inch long). (From drawings by Mr. J. Lawrence.) (E. A. S.)

A, a piece of the growing edge slightly magnified, showing the bony spicules terminated by bunches of osteogenic fibres; *a*, an isolated bony spicule united to the main part of the ossification by a bundle of osteogenic fibres.

B, the part marked *b* of the smaller figure, highly magnified; *sp*, bony spicules, with some of the osteoblasts imbedded in them, producing the lacunæ; *ost*, osteoblasts partly imbedded in the newly formed bone; *of*, osteogenic fibres prolonging the spicules, with osteoblasts between them and applied to them; *a*, granules of calcareous deposit between the osteogenic fibres; at *b* the granules have become blended, and the matrix is clearer; at *c* a continuity is established between the two adjacent spicules.

Some of the osteoblasts are involved in the ossifying matrix, and remain as the corpuscles of the future bone, the spaces enclosing them being the lacunæ. It is supposed that the canaliculi, which are at first short, are afterwards extended by absorption, so as to anastomose with those of neighbouring lacunæ.

It is believed by many histologists that the fibrillated ground-substance of bone is formed not outside the cells in an intercellular substance, but by a direct conversion of the protoplasm of some of the osteoblasts into bony tissue. If this were the case, there ought to be some indication in the formed osseous substance of the cell-areas of which it was made up, but nothing of the kind has been shown to exist. There should moreover often be observed osteoblasts which are only partly converted into bony substance, but this has also never been described. And if as some suppose, the peripheral part of each osteoblast becomes converted into osseous substance, while the central part and nucleus remain as the corpuscle within a lacuna, the osteoblasts would have to be originally far larger than the permanent lacunæ, which is certainly not the case. The view in question is similar to that which supposes ordinary connective tissue to have a like origin, and appears to rest more upon theory than on actual observation of the stages of the developmental process.

Meanwhile, the meshes of the bony network, which were occupied as we have seen by one or more blood-vessels, and by numerous osteoblasts, become diminished in extent, and the bone at the same time increased in thickness by the deposit upon the original trabeculæ of irregular bony laminæ and trabeculæ, some of the osteoblasts remaining, and forming the corpuscles and lacunæ as before. The interstices of the bony spongework thus becomes gradually narrowed, containing one or more blood-vessels surrounded by osteoblasts.

At a later stage the increase in thickness takes place by successive depositions of bony lamellæ under the periosteum, a concentric deposition occurring at the same time on the walls of the vascular channels. But since the growth in thickness of a membrane-bone takes place in exactly the same manner as that of one of the long bones, which will be fully described in a subsequent page, the reader is referred to the account of the process there given.

It may be observed that the appearance of the ossifying membrane-bone in the shape of a network of trabeculæ seems to be determined by the pre-existence of a vascular network in the embryonic tissue. The new bone everywhere makes its appearance in the spots which are furthest from the vessels, and the bony network everywhere alternates with the vascular network. At the edges of the advancing bone the spicules which prolong it pass between, and avoid the capillary blood-vessels, which are thus left in the bays between the spicules : the divergent bunches of osteogenic fibres which prolong the adjacent spicules complete the enclosure of the blood-vessel.

After a time the membrane-bone extends so as almost to come into contact with the neighbouring bones. But as long as growth continues, there always remains in the situation occupied afterwards by the sutures a vascular connective tissue with numerous osteoblasts. This is continually on the increase, but as fast as it grows, the osteogenic fibres and the osseous spicules extend into it from the young bones on either side. At length, however, when these have attained their full dimensions, the growth of the intermediate tissue ceases, and it becomes completely invaded by the bone on either side, with the exception of the narrow and irregular line of suture, which may eventually itself become more or less obliterated.

From a morphological point of view, the membrane-bones, especially those of the skull, are probably to be regarded as the modified remains of an integumental skeleton which is extensively developed in some of the lower vertebrata, and which had in all probability as its phylogenetic precursor a formation of dentinous, cutaneous spines. Even the membrane-formation in connection with the cartilage-bones may have originated in the same manner.

OSSIFICATION IN CARTILAGE.

It has already been stated that, in by far the greater number of bones the mesodermic tissue with closely packed cells, of which they originally consist, is very quickly succeeded by cartilage, in which the ossification begins. One of the long bones taken from a very small embryo, just before ossification has commenced

Fig. 310.—HUMERUS OF A FŒTUS, NATURAL SIZE. (Sharpey.)

The upper part is divided longitudinally. *a*, cartilage, *b*, line of junction of bone and cartilage. The periosteal bone looks lighter than the endochondral bone proper.

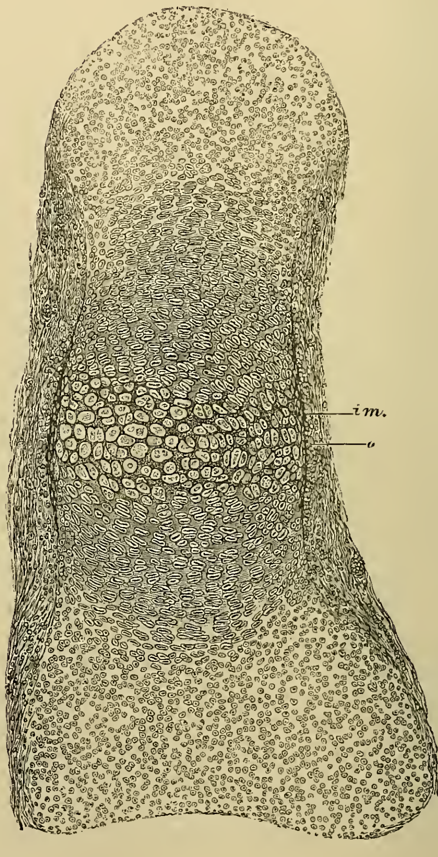


Fig. 311.—SECTION OF PHALANGEAL BONE OF HUMAN FŒTUS, AT THE TIME OF COMMENCING OSSIFICATION. Photographed from a preparation by Mr. F. A. Dixey. Magnified about 75 diameters. (E. A. S.)

The cartilage cells in the centre are enlarged and separated from one another by dark-looking calcified matrix ; *im*, layer of bone deposited underneath the periosteum ; *o*, layer of osteoblasts by which this layer has been formed. Some of the osteoblasts are already embedded in the new bone as lacunæ. The cartilage-cells are becoming enlarged and flattened and arranged in rows above and below the calcified centre. At the ends of the cartilage the cells are small and the groups are irregularly arranged ; the fibrous periosteum is not sharply marked off from the cartilage.

in it, is observed to be distinctly cartilaginous. In the tibia of a sheep, for example, at a time when the whole embryo is not more than an inch and a quarter in length, we can plainly see that the substance consists of cartilage-cells imbedded in a pellucid matrix. These cells can scarcely be said to be collected into groups, and are very irregular in size and shape. They become enlarged in the middle part of

the shaft when ossification is about to commence. As it grows, the cartilage acquires firmer consistence; it represents in figure the future bone, though of course much smaller in size, and it is surrounded with a fibrous membrane, the future periosteum. Vessels ramify in this membrane, but none are seen in the cartilage until ossification is about to begin. In a long bone the ossification commences in the middle and proceeds towards the ends, which remain long cartilaginous, as represented in fig. 310. Much later, separate points of ossification appear in them, and form epiphyses, which at last are joined to the body of the bone.

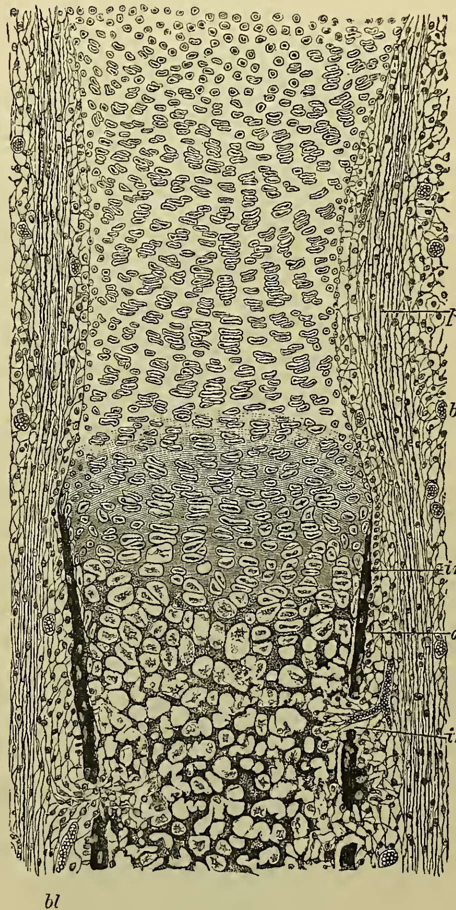


Fig. 312.—Section of part of one of the limb bones of a fœtal cat, at a more advanced stage of ossification than is represented in fig. 311, and somewhat more highly magnified. (Drawn by Mr. J. Lawrence.) (E.A.S.)

The calcification of the cartilage matrix has advanced from the centre, and is extending between the groups of cartilage-cells which are now arranged in characteristic rows. The subperiosteal bony deposit (*im*) has extended *pari passu* with the calcification of the cartilage matrix. The cartilage cells in the primary areolæ are mostly shrunken and stellate, in some cases they have dropped out of the space. At *ir* and in two other places an irruption of the subperiosteal tissue, composed of ramified cells with osteoblasts and growing blood-vessels, has penetrated the subperiosteal bony crust, and has begun to excavate the secondary areolæ or medullary spaces; *p*, fibrous layer of the periosteum; *o*, layer of osteoblasts, some of them are embedded in the osseous layer as bone-corpuscles in lacunæ; *bl*, blood-vessels occupied by blood-corpuscles. Beyond the line of ossific advance the periosteum may be noticed to be distinctly incurved. This incurvation is gradually moved on, the cartilage expanding behind it until the head of the bone is reached, when it forms the periosteal notch or groove represented in fig. 313, *p*.

The manner in which the process of ossification of a cartilage bone takes place is as follows :—

In the middle of the cartilage the cells are enlarged, and are separated from one another by a relatively larger amount of matrix than elsewhere (fig. 311). This matrix becomes hardened by calcareous deposit, assumes a granular opaque appearance, and has a gritty feel to the knife. Meanwhile the cartilage-cells above and below the centre of ossification become enlarged and flattened, and piled up in elongated groups or columns which radiate from the centre for a certain distance towards either end. The columns taper towards their ends, where the cartilage-cells which compose them are smaller. Into the matrix between these oblong groups the calcareous deposit extends between and around the groups of cells, so that the calcified substance encloses the columns; the cell-spaces in the calcified matrix

which are still occupied by the cartilage-cells, either singly or in elongated groups, being termed the *primary areolæ* (Sharpey). Simultaneously with this deposit in the cartilage-matrix, a layer of osseous substance (fig. 311, *im*) is becoming formed on the outside of the cartilage underneath the periosteum. This last is a vascular membrane, containing numerous osteoblasts (*o*), which are chiefly collected on the

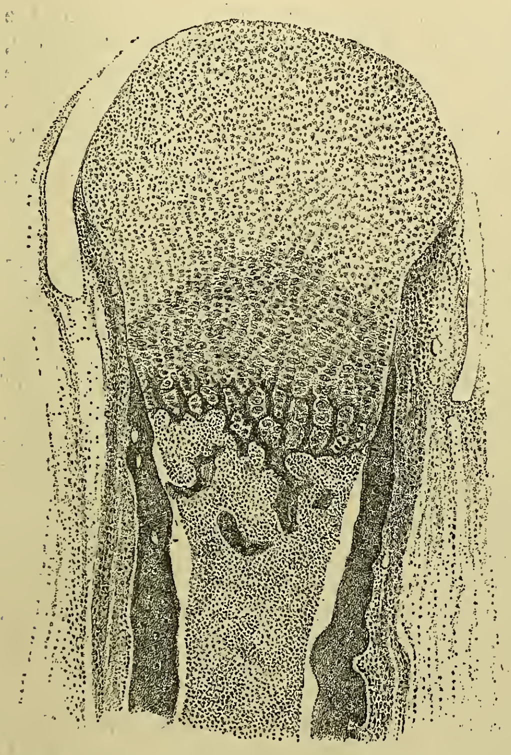
Fig. 313.—LONGITUDINAL SECTION THROUGH THE UPPER HALF OF THE DECALCIFIED HUMERUS OF A FŒTAL SHEEP, AS SEEN UNDER A MAGNIFYING POWER OF ABOUT 30 DIAMETERS. (Drawn by Mr. J. Lawrence.) (E.A.S.)

ic, the part of the shaft which was primarily ossified in cartilage; what remains of the primary bone is represented as dark, enveloped by the clear secondary deposit. The areolæ of the bone are occupied by embryonic marrow with osteoblasts, and blood-vessels variously cut, represented as dark lines. One long straight vessel (*bv*) passes in advance of the line of ossification far into the cartilaginous head, most of the others loop round close to the cartilage. At one or two places in the older parts of the bone elongated groups of cartilage-cells (*c*) may still be seen which have as yet escaped absorption. *im*, the part of the bone that has been ossified in membrane, that is to say in the osteoblastic tissue under the periosteum. It is well marked off from the central portion, and is bounded, peripherally, by a jagged edge, the projections of which are indistinctly seen to be prolonged by bunches of osteogenic fibres. A row of osteoblasts covers the superficial layer of the bone. The subperiosteal layer is prolonged above into the thickening (*p*), which encroaches upon the cartilage of the head of the bone, and in which are seen, amongst numerous osteoblasts and a few blood-vessels, the straight, longitudinal osteogenic fibres (*of*), and some other fibres (*pf*) crossing them, and perhaps representing fibres of Sharpey. The calcareous salts having been removed by an acid, the granular ossific deposit passing up between the rows of cartilage-cells is not seen in this specimen. Observe the general tendency of the osseous trabeculæ and the vascular channels between them to radiate from the original centre of ossification. This is found to prevail more or less in all bones when they are first formed, although the direction of the trabeculæ may afterwards become modified in relation with varying physiological conditions, and especially as the result of pressure in different directions.

inner surface next to the cartilage, and it is by their agency that the bony layer on the surface of the cartilage is formed and becomes increased both in thickness and length. The bony layer, when viewed on the surface, shows the usual component fibres of bony lamellæ, and as other layers are deposited upon it lacunæ become formed between them by the inclusion of some of the osteoblasts. In this first stage of ossification, we see therefore two processes going on, a deposit of earthy

matter in the matrix of the cartilage, the cells of which assume a highly characteristic arrangement, and a deposition of true membrane-bone, underneath the perichondrium, and closely investing the surface of the cartilage.

What next happens is an irruption of the subperiosteal vascular and osteoblastic tissue into the middle of the cartilage, one or more apertures being excavated by absorption in the newly deposited osseous lamella and the tissue in question passing through these and burrowing into the cartilage (fig. 312, *ir*). Here it absorbs a great part of the calcified matrix, and by demolishing in this way parts of the walls



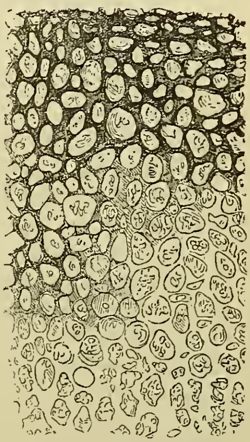


Fig. 315.—Transverse section of ossifying cartilage, including a portion of the advancing calcification. From the humerus of a fœtal sheep, magnified 70 diameters. (Sharpey.)

c, cartilage, the cells of which are enlarged, but the matrix not yet calcified; *b*, primary osseous deposit in the cartilage-matrix, extending between the cartilage-cells and enclosing them in primary areolæ.

Fig. 314.—Longitudinal section through part of a phalanx of a 6 months' human embryo. (Kölliker.)

The calcified cartilage is completely absorbed almost to the limit of advancing ossification. The darker substance on either side is the periosteal bone. The embryonic marrow has shrunk somewhat away from it.

of the primary areolæ, forms larger spaces (the *secondary areolæ* of Sharpey, the *medullary spaces* of H. Müller) which are filled by jelly-like embryonic marrow, with ramified cells and osteoblasts, the cartilage-cells which occupied the primary areolæ disappearing before it. All the middle of the calcified temporary cartilage becomes thus excavated with large spaces and replaced by the vascular osteoblastic tissue. As the calcification of the cartilage-matrix extends towards the ends of the shaft, proceeding always in the same manner, the osteoblastic tissue closely follows, and after supplanting the cartilage-cells in the primary areolæ, absorbs parts of their walls so as to throw two or more together to form secondary areolæ; in this way a great part of the primary bone (or calcified cartilage-matrix) is at once removed.

At a short distance below the advancing ossification, the medullary spaces become at first somewhat more enlarged by further absorption, but at the same time

their walls (which were at first formed only by the remains of the walls of the primary areolæ and therefore only by calcified cartilage-matrix) begin to be thickened by the deposition of layers of new bone, and this deposition increases gradually towards the middle of the shaft (compare fig. 317, *c* and *d*). The lacunæ first appear in this deposit, there are of course none in the calcified cartilage. Moreover as layer after layer is deposited upon the walls of the medullary spaces these become gradually narrowed into inter-communicating channels, which contain little more than a blood-vessel and some jelly-like embryonic connective tissue (fœtal marrow) with a few osteoblasts applied to the bone.

In the end, some of the enlarged cavities and their walls remain to form the cancellated tissue, but much of this structure is afterwards removed by absorption, to give place to the medullary canal of the shaft. In many of the cavities the walls of the coalesced primary areolæ may long be distinguished, like little arches, forming by their union a sort of festooned outline, upon which the new bony laminæ are deposited (see fig. 318, and fig. 305, *c*).

In some of the smaller bones it may happen that the calcified cartilage is completely absorbed from the centre of the shaft before any new deposition of bone takes place. This is the case in the phalanges (fig. 314).

The *primary osseous matter* forming the original thin walls of the areolæ, and produced by calcification of the cartilaginous matrix, is decidedly granular, and has a dark appearance ; the subsequent or *secondary deposit* on the other hand is quite transparent, and of a uniform, homogeneous aspect. This secondary deposit begins to cover the granular bone a very short distance below the surface of ossification (see fig. 317), and, as already stated, increases in thickness further down.

Close to the limit of advancing ossification, the blood-vessels terminate in capillary loops (see figs. 313, 317), which are often somewhat dilated. It is supposed by Ranvier that these vascular loops by their growth directly produce absorption of the cartilage, but it is more probable that this is caused by the agency of some of the cells which accompany the blood-vessels. The absorption of the walls of the primary areolæ (calcified cartilage-matrix) seems to be effected by certain large cells (fig. 317, *f*, *f*) which from their function have been termed by Kölliker, *ostoclasts*, and which are found wherever bone is being eaten away: we shall return to them further on. The secondary bone which thickens the walls of the medullary spaces is no doubt formed by the osteoblasts.

With regard to the destination of the cartilage-cells, two opposite views have been taken by histologists. According to one, which was that adopted by H. Müller, and has received most adherence, the capsules are opened by absorption, and the cells are converted, after undergoing division, into osteoblasts. According to the other, the cartilage-cells themselves become removed by absorption, and take no part, directly or indirectly, in the production of the secondary bone. The latter view of the matter was taken by Lovén, and it was also regarded by Sharpey as in all probability the more correct.

It is difficult to decide between these views. All that can be said is that the line of demarcation between the cartilage-cells and the osteoblastic tissue is exceedingly abrupt (fig. 317), and that the latter often, if not always, terminates either by a dilated vascular loop, or it may be by a developing capillary filled with blood corpuscles. Except that they are generally much shrunken and irregular in form (at least after death or the action of reagents), the cartilage-cells show no absorption and no distinct evidence of division, and it may be remarked that this is also the case when, as sometimes happens, they have not disappeared before the advancing subperiosteal tissue, but remain for a time still occupying an untouched primary areola (see fig. 313, *c*).

As ossification advances towards the ends of the bone, the portion as yet

cartilaginous continues to grow at the same time, increasing in every dimension. The part already osseous increases also in circumference; fresh bone being continually deposited in the subperiosteal membranous tissue outside that which is first formed on the surface of the cartilage (figs. 313, 318). The subperiosteal

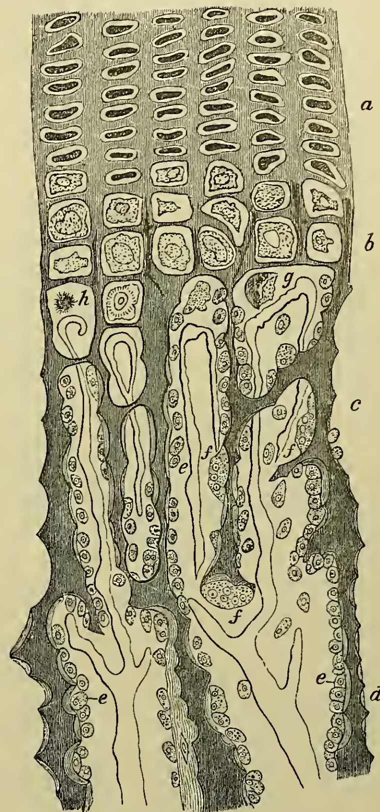


Fig. 316.—Small portion of a section of developing bone, taken at the junction of the bone and cartilage, and examined in the fresh condition. Magnified about 140 diameters. (Sharpey.)

a, *b*, two of the new-formed osseous tubes or areolæ, with a few shrunken cartilage-cells lying in them; *c*, cartilage-cells near the ossifying surface, large and clear and filling the cavities in the matrix; on the left of the figure some of them are shrunken.

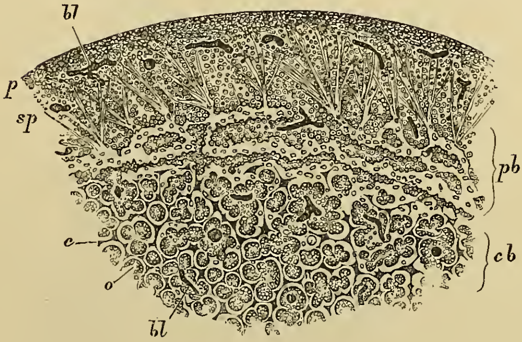
Fig. 317.—Part of a longitudinal section of the developing femur of the rabbit. Drawn under a magnifying power of 350 diameters (from Klein and Noble Smith).

a, rows of flattened cartilage-cells; *b*, greatly enlarged cartilage-cells close to the advancing bone, the matrix between is partly calcified; *c*, *d*, already formed bone, the osseous trabeculæ being covered with osteoblasts (*e*), except here and there, where a giant-cell or ostoclast (*f*), is seen, eroding parts of the trabeculæ; *g*, *h*, cartilage-cells which have become shrunken and irregular in shape. From the middle of the figure downwards the dark trabeculæ, which are formed of calcified cartilage matrix, are becoming covered with secondary osseous substance deposited by the osteoblasts. The vascular loops at the extreme limit of the bone are well shown, as well as the abrupt disappearance of the cartilage-cells.

deposit takes place in the same way as in the formation of a membrane bone. Bony spicules prolonged by bunches of osteogenic fibres (fig. 318) project out from the previously formed layer, into the intervals between the blood-vessels. By the union of the spicules the vessels become in like manner enclosed in channels whose walls are gradually thickened by deposits of osseous substance, between which some of

the osteoblasts are left behind as bone-corpuscles in lacunæ, whilst others remain surrounding the blood-vessels within the meshes.

The question whether bone can be directly formed from cartilage by a transformation of the cartilage-matrix into osseous tissue, whilst the cartilage-cells become bone-corpuscles (metaplastic ossification), is one which has been much discussed of late years and can hardly as yet be said to be definitely decided. But although the cells of a calcified cartilage in the neighbourhood of advancing ossification sometimes appear stellate and simulate bone-corpuscles, and the calcified fibrous matrix



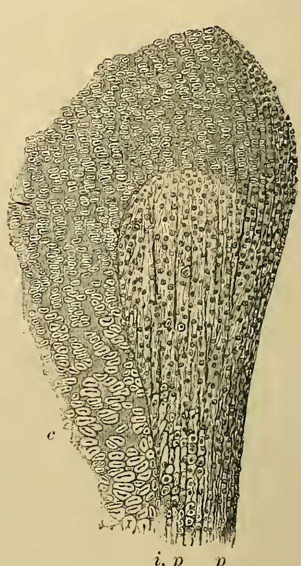


Fig. 318.—Part of a transverse section of a developing long bone, rather more advanced than that represented in fig. 313, and under a higher magnifying power (E. A. S.). From a drawing by Mr. J. Lawrence.

cb, endochondral bone which began as a calcification of the cartilage-matrix, parts of which still remain (*c*) covered over by secondary osseous deposit ; *o*, secondary areolæ, occupied by vessels, fœtal marrow, and osteoblasts ; *pb*, periosteal bone deposited in the form of irregular trabeculæ, prolonged externally by bony spicules passing into bunches of osteogenic fibres. These, which are everywhere covered with osteoblasts, become lost in the external fibrous layer of the periosteum, *p* ; *bl*, *bl*, blood-vessels variously cut.

Fig. 319.—Longitudinal section through the periosteal thickening of a bone at about the same stage of development as that represented in fig. 313. From a drawing by Mr. J. Lawrence. (E. A. S.)

c, cartilage with the cells in rows ; the tissue of the periosteal thickening is sharply marked off from it except near the surface ; *p*, outer layer of the periosteum ; *i*, *p*, inner layer of the periosteum or subperiosteal tissue, with osteogenic fibres, and osteoblasts. One or two blood-vessels are observed cut across.

of the cartilage may in like manner simulate osseous tissue, there is not sufficient evidence to show that true lamellar bone is formed in any other way than through the agency of osteoblasts.

The first formed bony tissue is different in its general appearance from the bony tissue of the adult, being reticular and not regularly lamellar, and, for a long while, even the shafts of the long bones are rather cancellated, than compact in their texture. The more obviously lamellated condition does not begin to appear until about the sixth month after birth, when the periosteum deposits a succession of entire lamellæ around the embryonic bone. The blood-vessels which pass from

the periosteum into the bone, pierce these circumferential lamellæ, but are not at first surrounded with concentric lamellæ, and do not therefore lie in true Haversian canals.[1] These canals become formed later by absorption taking place around the blood-vessels for some little distance, succeeded by a re-deposition of concentric lamellæ within the Haversian spaces thus formed.

Immediately before the occurrence of the lamellar deposition under the periosteum, the young bone undergoes a process of absorption from the inside. The medullary canal becomes thereby enlarged, and the medullary spaces, particularly those near the medullary canal, partaking of this absorption and enlargement, the result is that at about this period there is less bony matter in a section of the shaft than there was immediately before. To the change in question Schwalbe has given the name "osteoporosis;" it is followed by a re-deposition of osseous lamellæ both on the wall of the medullary canal, and on the walls of the medullary spaces of the embryonic osseous tissue.

Since the cartilage grows in every dimension by interstitial expansion, the bone which is invading it (endochondral bone) becomes gradually wider as the ossification advances. It is narrowest near the centre of the shaft where the process began, and widens gradually towards the ends; it has therefore somewhat of an hour-glass shape (fig. 313, *i.c.*). The cylindrical form of the shaft is maintained, however, by the thickness of the periosteal bone being greater at the centre (where the deposition of bone first began, and has been longest proceeding) than at the ends. Hence it gradually diminishes to a thin layer immediately investing that part of the cartilage into which the calcification is extending, so that the intramembranous subperiosteal ossification on the outside, may be said to closely accompany, if it does not even precede, the calcification of the cartilage in the interior. Either this investment of periosteal bone, or the calcification of the cartilage, seems to hinder the lateral expansion of that part of the cartilage in which the calcification is proceeding; but immediately beyond, the interstitial expansion mentioned takes place. By the time that the ossification has advanced to the extremities of the shaft, the enlarged and expanded end of the cartilage has extended itself over the subperiosteal layer, so that this, with the accompanying osteoblastic tissue, now seems to lie in a groove or notch (fig. 313, *p*) in the cartilaginous head of the bone (Ranvier). This groove is filled with the same tissue as that which underlies the rest of the periosteum, namely, a vascular tissue with branched cells and osteoblasts and osteogenic fibres. The latter are prolonged from the periosteal bone, and have for the most part a longitudinal direction (fig. 319). The tissue which fills this periosteal notch appears to become gradually converted by a metaplastic process into cartilage in the same way as the superficial part of a rib cartilage is formed by conversion of the deeper layers of the perichondrium (see p. 253). Thus, besides the interstitial growth and expansion of the cartilaginous end, there is a constant new formation of cartilage going on at its surface.

Blood-vessels extend from the newly-formed osseous tissue beyond it into the cartilage. The vessels are lodged in excavations or branching canals in the cartilage (fig. 313), which also contain granular corpuscles (? osteoblasts). Other vascular canals enter the cartilage from its outer surface, and conduct vessels into it directly from the perichondrium.

The formation of osseous tissue, having thus proceeded for some time in the shaft, at length begins in the extremities of the bone from one or more independent centres, and extends through the cartilage, leaving, however, a thick superficial layer of it unossified, which permanently covers the articular ends of the bone. The

[1] Even in the adult bone it may often be noticed that the blood-vessels which pierce the superficial lamellæ are not enclosed by Haversian systems (see pp. 257—8).

epiphyses thus formed are separated, as long as growth continues, from the shaft or diaphysis by an intervening portion of cartilage, which is at last ossified, and the bone is then consolidated.

A remarkable exception to the ordinary mode of ossification of the cartilage-bones occurs in the terminal phalanges of the digits. In these the calcification of the cartilage begins at the distal extremity or tip, and the sub-periosteal deposit appears simultaneously at the same point, and forms a cap-like expansion over the end of the phalanx. The irruption of the osteoblastic tissue also first occurs at this place. The expanded portion of the phalanx which bears the nail is formed independently of cartilage (Dixey).

Growth and absorption of bone.—The time of final junction of the epiphyses is different in different bones; in many it does not arrive until the body has reached its full stature. Meanwhile, as above described, the bone increases in length by the ossification continuing to extend into the intervening cartilage, which goes on growing at the same time; and it appears that in the part of the shaft already ossified little or no elongation takes place by interstitial growth.[1] This is shown by an experiment first made by Hales and afterwards by Duhamel and by John Hunter, in which, two or more holes being bored in the growing bone of a young animal at a certain measured distance from each other, they are found after a time not to be farther asunder, although the bone has in the meanwhile considerably increased in length. On the other hand, if one hole be bored in the epiphysis and another in the shaft, they become distinctly removed from one another with the growth of the bone. Moreover, it is well known that if the intervening cartilage in growing bone be injured by disease or removed by the knife, the growth of the bone in length permanently ceases.

Both Hales and Duhamel in experimenting on the growing tibia of a chicken, observed that the elongation was much greater at the upper end. Humphry has shown that in the arm-bones the elongation is greater at the end furthest from the elbow joint, and in the leg-bones at the end which is next the knee joint.

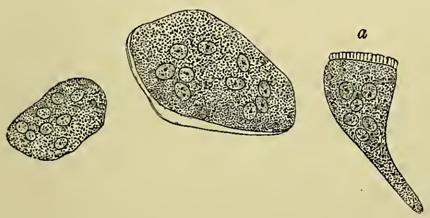
In the human subject between the first and the fourth or fifth years, the long bones grow chiefly in length, scarcely at all in thickness.

The shaft of a long bone increases in circumference by deposition of new bone on its external surface, while at the same time its medullary canal is enlarged by absorption from within. This can be determined by two methods of experimenting. Thus, in the first place, a ring of silver or platinum put round the wing-bone of a growing pigeon, becomes covered with new bone from without, and the original bone included within it gets thinner, or, according to Duhamel, who first made the experiment, is entirely removed, so that the ring comes to lie within the enlarged medullary canal. Secondly, madder given to an animal along with its food tinges those parts in which deposition of new bone is taking place. The earth of bone appears to act as a sort of mordant, uniting with and fixing the colouring matter; and, as in this way the new osseous growth can be readily distinguished from the old, advantage was taken of the fact by Duhamel, and afterwards by Hunter, in their inquiries as to the manner in which bones increase in size. By their experiments it was shown that when madder is given to a young pig for some weeks, the external part of its bones is deeply reddened, proving that the new osseous matter is laid on at the surface of that previously formed. Again, it was found that, when the madder was discontinued for some time before the animal was killed, an exterior white stratum (the last formed) appeared above the red one, whilst the internal white part, which was situated within the red, and had been formed before any madder was given, had

[1] The occurrence of a certain amount of interstitial expansion is strenuously upheld by J. Wolff (see Bibliography).

become much thinner; showing that absorption takes place from within. In this last modification of the experiment also, as noted by Hunter, a transverse red mark is observed near the ends of the bone, beyond which they are white; the red part indicating the growth in length during the use of the madder, and the white beyond, that which has taken place subsequently,—thus showing that the increase in length is caused by the addition of new matter to the extremities. Madder administered while the process of formation of the concentric lamellæ of the Haversian systems is going on, colours the interior and recently-formed laminæ, so that in a cross section the Haversian apertures appear surrounded with a red ring.

Flourens, and more recently, Kölliker, have repeated and varied these experiments, and have represented the results in beautiful delineations. Kölliker has, in addition, carefully investigated the microscopic appearances observed in the process of absorption of bone. From the results of his researches (which were in part anticipated by those of Lovén), it would seem that the process is essentially dependent on the presence of large multi-nucleated cells, by him termed "ostoclasts," identical with the "myeloplaxes" of Robin (see p. 267), which excavate, in



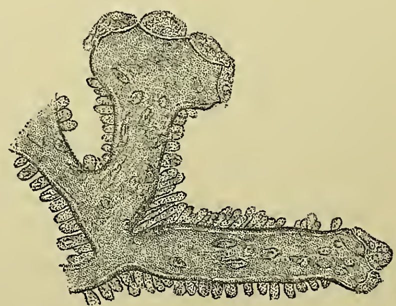


Fig. 320.—Three ostoclasts from absorption surfaces of growing bone. 400 diameters (Kölliker).
a, with thickened striated border.

Fig. 321.—Bony trabecula from the lower jaw of a calf embryo with Howship's foveolæ and giant-cells at the ends where absorption is proceeding and osteoblasts covering the sides where bone is being deposited (Kölliker).

the part which is undergoing absorption, small shallow pits (*foveolæ*) in which also they lie. These pits were first noticed by Howship: they seem to occur wherever absorption is proceeding, and it is to them that the festooned appearance of the Haversian spaces (p. 264) is due. The ostoclasts (figs. 320, 321) vary in size, but are always many times larger than a blood-corpuscle: in shape they are spheroidal or flattened, with either an even or an irregular outline. Their substance is granular in appearance, and they each contain from two to ten clear round nuclei, but this number may be considerably exceeded, whilst on the other hand, there may be but one large nucleus provided with a number of bud-like projections. The ostoclasts have frequently on the side by which they are in contact with the bone a thickened striated border (fig. 320, *a*), somewhat similar to the well-known thickened base of the columnar epithelium-cells of the intestine. With respect to the origin and destiny of the ostoclasts, they are regarded by Kölliker both as in the first instance derived from and as eventually breaking up into osteoblasts. Ostoclasts are found in connection with the roots of the milk teeth where these are undergoing absorption to make way for the permanent set. They were also noticed by Billroth to produce absorption of ivory pegs which had been driven into bone. Precisely

similar cells occur under pathological conditions in various situations apart from any hard tissue, and have long been known as "giant-cells" (*Riesenzellen*, Virchow).

The changes of shape which the bones undergo in the process of growth, as well as any changes which may occur in them in adult life, are all produced in the same manner as the increase of size—that is to say, not by interstitial growth and expansion of the substance of the bone in one direction more than in another, but by a deposition of new bone by osteoblasts at some parts and a simultaneous absorption by ostoclasts at others; whilst in other places again neither absorption nor deposition is occurring—just as a modeller corrects his work by laying clay on at one part whilst removing it at another.[1]

Since during the growth of bones their shape is becoming continually altered, it follows that in nearly all bones during growth there are parts of the bone which are in process of absorption, and others which are in process of more active deposition than the rest. In most of the long bones, towards their ends, absorption is generally taking place at one side, and deposition on the opposite side. The former process may, and probably does, proceed to such an extent, that the endochondral bone may be laid bare or even partially absorbed, but after a while, when the absorption has ceased at any part, re-deposition may take place, the ostoclasts being replaced by osteoblasts, and successive circumferential lamellæ being deposited by these.

A large amount of variation is met with in the different bones of the skeleton in the relative extent to which they are formed in cartilage and in the sub-periosteal tissue respectively. Whereas in some, such as the shafts of the long bones of the limbs, the endochondral bone is almost entirely removed, as we have seen, and periosteal bone substituted for it; in others, such as the bodies of the vertebræ, and the epiphyses of the long bones, a much larger proportion of the adult bone has had an endochondral formation. In one or two bones or parts of bones again, which may be said to have typically an intramembranous origin, cartilage may, according to Kassowitz, become developed under the periosteum at certain places, and the continuation of the ossification may occur in this secondarily developed cartilage. This is said to be the case with the clavicle, the foundation of which is laid in membrane, but which is found at a later period to have cartilaginous ends; and also with the halves of the lower jaw-bone, which develops cartilaginous ends both towards the symphysis and towards the articular and coronoid processes, these cartilaginous ends being altogether distinct from the cartilage of Meckel, which at those parts is unconnected with the jaw-bone, although at another place (in front) it is involved in the ossification of the maxilla (see vol. ii., p. 78). Kassowitz has described similar cartilaginous developments in connection with the sub-periosteal tissue at the tuberosity of the radius and the spine of the scapula. They are merely an extension of the process which normally goes on at the ossification groove (p. 279).

The time of commencement of ossification in the different bones, as well as the number and mode of conjunction of their centres of ossification, are treated of in the Descriptive Anatomy (vol. ii.).

Regeneration of bone.—In the reunion of fractured bones, osseous matter (often preceded by a new formation of cartilage), is formed between and around the broken ends, connecting them firmly together; and when a portion of bone dies, a growth of new bone very generally takes place to a greater or less extent, and the dead part is thrown off. The importance of the periosteum in the process of repair is shown by the fact that if a portion of periosteum be stripped off, the subjacent

[1] For special details of this modelling process as it is met with in the different bones of the skeleton, the reader is referred to Kölliker's memoir; Die normale Resorption des Knochengewebes. Leipzig, 1873; and to a paper by Kassowitz (Die normale Ossification, &c.) in Stricker's Med. Jahrb. 1879—1880.

bone will be liable to die and exfoliate ; conversely, if a large part or the whole of a bone be removed and the periosteum at the same time be left intact, the bone will, in a great measure, be regenerated. Osseous formation will even occur in connection with portions of periosteum which have been stripped away from the bone itself and intertwined amongst the muscles of the part, or even with portions that have been entirely removed from a bone and transplanted to a soft tissue (Ollier).

It is doubtful if the marrow-tissue can assist in the regeneration of bone. Experiments which have been made to determine this point would seem to show that although in the young bone, where the osteoblasts still retain their osteogenic function, the medullary tissue may take an active part in the formation of the first-formed new bone or "callus," in the adult no such participation of the marrow in the regeneration of bone takes place.

In the young subject even small pieces of the bone itself can be transplanted, and McEwen has succeeded in renewing the greater part of the excised humerus of a child by the introduction, at successive periods, of portions of fresh bone removed from another patient.

It was long supposed that all the bones of the skeleton were preceded by and deposited in cartilage. Nesbitt, however, showed in 1736 that some of the flat bones were formed independently of cartilage, and he further maintained that the cartilage is "entirely destroyed ;" he therefore considered it to be a mere temporary substitute ; but the steps of the process of intracartilaginous ossification as now traced with the aid of the microscope were unknown to him, and it was not until the year 1846 that the manner of formation of bone and the extensive replacement of the primarily ossified cartilage by new bone formed in membrane was made clear by the researches of Sharpey, who published the results of his work in the fifth edition of this book.

RECENT LITERATURE.

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MUSCULAR TISSUE.

The muscular tissue is that by means of which the active movements of the body are produced. It consists of fibres, which are for the most part collected into distinct organs called "muscles," and in this form it is familiarly known as the flesh of animals. These fibres, from a characteristic appearance which they exhibit under the microscope, are usually known as "cross-striped" or "striated;" they are many of them under the control of the will, and are hence often spoken of as "voluntary" muscles. Another kind of muscular tissue is disposed around the blood-vessels and most of the hollow viscera, often forming a distinct coat or coats to these. In this kind the fibres do not exhibit the same cross-striated appearance, and they have therefore been termed in contradistinction "plain" or "non-striated" muscular fibres. Most of these are entirely withdrawn from the control of the will, and they are therefore also termed involuntary. The muscular tissue of the heart, although having a cross-striated appearance, differs in many respects from that of the skeletal muscles: it is therefore described separately under the term "cardiac" muscular tissue. Muscular fibres are endowed with contractility, by virtue of which they shrink or contract more or less rapidly under the influence of certain causes which are capable of exciting or calling into play the property in question, and which are therefore named stimuli.

STRUCTURE OF CROSS-STRIATED OR SKELETAL MUSCLES.

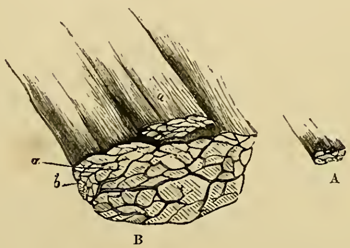
The skeletal muscular fibres are for the most part gathered into distinct organs or muscles of various sizes and shapes, but most generally of an oblong form, and furnished with tendons at each extremity, by which they are fixed to the bones.

The fibres are in the first place collected into bundles, of greater or less thickness, named *fasciculi* or *lacerti* (fig. 322). The fibres are parallel in the fasciculi; and the fasciculi extend continuously from one terminal tendon to the other, unless in those instances, like the rectus muscle of the abdomen and the digastric of the inferior maxilla, in which the fleshy part is interrupted by interposed tendinous tissue. The fasciculi also very generally run parallel, and, although in many instances they converge towards their tendinous attachment with various degrees of inclination, yet in the voluntary muscles they do not interlace with one another.

An outward investment or sheath of areolar tissue (*epimysium*) surrounds the entire muscle, and sends partitions inwards between the fasciculi; furnishing to each of them a special sheath (*perimysium*).[1] The areolar tissue extends also between the fibres (*endomysium*), but does not afford to each a continuous investment, and therefore cannot be said to form sheaths for them. Every fibre, it is true, has a tubular sheath; but this, as will be afterwards explained, is not composed of areolar tissue. The perimysium contains elastic as well as white fibres; but the elastic element is found principally in its investing, as distinguished from its penetrating, portion. In the endomysium numerous plasma-cells are found. The chief uses of the areolar tissue are to connect the fibres and fasciculi together, and to conduct and support the blood-vessels and nerves in their ramifications between the parts. The relation of these different subdivisions of a muscle to each other, as well as the shape of the fasciculi and fibres, is well shown in transverse section (figs. 322 and 323).

[1] The term *perimysium* has usually been employed to designate the external investment of the whole muscle as well as the special sheath of each fasciculus. I have ventured, however, to introduce the word *epimysium* for the general sheath, since the terms will then have a close analogy with those which are applied to the connective tissue investments of a nerve (see p. 324).

Fasciculi.—The fasciculi are of a prismatic figure, and their sections have therefore an angular outline (fig. 322). The number of fibres of which they consist varies, so that they differ in thickness, and a large fasciculus may be divisible into two or three orders of successively smaller bundles, but of no regularly diminishing magnitude. Some muscles have large, others only small fasciculi ; and the coarse or fine texture of a muscle, as recognized by the dissector, depends on this circum-



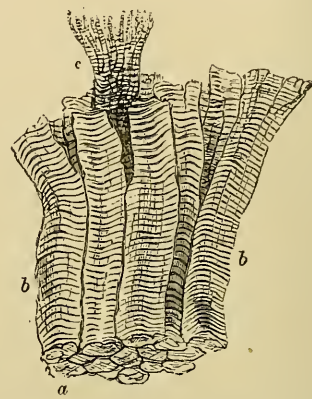


Fig. 322.—A, SMALL PORTION OF MUSCLE, CONSISTING OF LARGER AND SMALLER FASCICULI, NATURAL SIZE ; B, THE SAME MAGNIFIED 5 DIAMETERS, SHOWING A TRANSVERSE SECTION. (Sharpey.)

Fig. 323.—A FEW MUSCULAR FIBRES, BEING PART OF A SMALL FASCICULUS, MORE HIGHLY MAGNIFIED. (Sharpey.)

b, *b*, fibres ; *a*, end view ; *c*, a fibre splitting up into longitudinal elements.

stance. The length of the fasciculi is not always proportioned to the length of the muscle, but depends on the arrangement of the tendons to which their extremities are attached. When the tendons are limited to the ends of a long muscle, as in the sartorius, the fasciculi, having to pass from one extremity to the other, are of great length ; but a long muscle may be made up of a series of short fasciculi attached obliquely to one or both sides of a tendon, which advances some way upon the surface or into the midst of the fleshy part, as in the instances of the rectus muscle of the thigh, and the tibialis posticus. Many short fasciculi connected thus to a long tendon, produce by their combined operation a more powerful effect than a few fasciculi running nearly the whole length of the muscle ; but by the latter arrangement the extent of motion is greater, for the points of attachment are moved through a longer space.

Fibres ; their figure and measurement.—In shape the fibres are cylindrical, or prismatic with rounded angles. Their diameter varies greatly even in each muscle, although for the most part a prevailing standard is found to exist in every muscle. The largest fibres in human muscles average about $\frac{1}{250}$ inch (0·1 mm.) in diameter, the smallest are only about one-tenth that width.

The eye-muscles are mainly composed of small fibres ; and the muscles of the limbs mainly of larger ones, but there is no constant relation between the size of a muscle and that of its constituent fibres. The fibres tend to be thicker in the male than in the female (for the same muscles) ; the differences between different muscles are not evident in infancy, but only manifest themselves in the process of growth (Schwalbe and Mayeda).

The fibres composing a muscle are of limited length, generally not exceeding one inch and a half ; and accordingly in a long fasciculus a fibre does not reach from one tendinous attachment to the other, but ends with a rounded or tapering extremity, invested with its sarcolemma, and cohering with neighbouring fibres. Unless when

either is fixed to a tendon, both extremities of the fibre terminate in the way described, so that it has a long cylindrical shape, but when provided with tapering ends it becomes somewhat spindle-shaped. In some muscles, e.g., the sartorius, fibres have been measured which are much longer than the dimension above given.

Generally speaking the fibres neither divide nor anastomose ; but this rule is not without exception. In the tongue of the frog the muscular fibres (fig. 324) as they approach the surface divide into numerous branches, by which they are attached to the under surface of the mucous membrane (Kölliker). The same thing has also been seen in the tongue of man and various animals : and the fibres of the facial muscles of mammals divide in a similar manner where they fix themselves to the skin (Busk and Huxley).

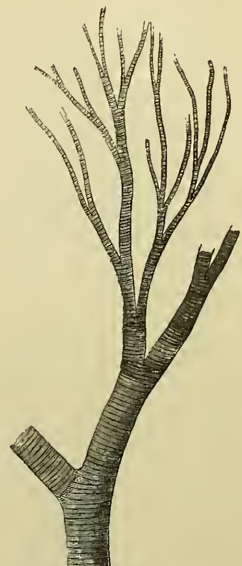


Fig. 324.—A BRANCHED MUSCULAR FIBRE FROM THE FROG'S TONGUE, MAGNIFIED 350 DIAMETERS. (Kölliker.)

Structure of the fibres ; sarcolemma.—A muscular fibre may be said to consist of a soft substance enclosed in a tubular sheath. The latter is named the *sarcolemma.* It consists of transparent and apparently homogeneous elastic membrane, and, being comparatively tough, will sometimes remain entire when the included muscular substance is ruptured, as represented in figs. 325, 326. It is especially well seen in fish and amphibia, for in these it is thicker and stronger than in mammalian muscle, in which it is more difficult to render evident but nevertheless always exists (fig. 326). Nuclei are found on the inner surface of the sarcolemma, but these belong rather to the contractile substance than to the inclosing membrane, and will be afterwards more fully described.

Fig. 325.—MUSCULAR FIBRE OF FISH. SUBSTANCE OF FIBRE RUPTURED SO AS TO EXHIBIT SARCOLEMMA. (After Bowman.)

Muscular substance.—When viewed by transmitted light even with a comparatively low power of the microscope, the fibres, which are clear and pellucid in aspect, appear marked with parallel stripes or bands alternately light and dark passing across them with great regularity (fig. 327), and this not only at the surface but,

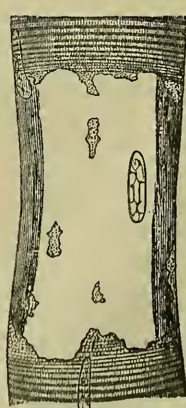


Fig. 326.—SARCOLEMMA OF MAMMALIAN MUSCLE, HIGHLY MAGNIFIED. (E. A. S.)

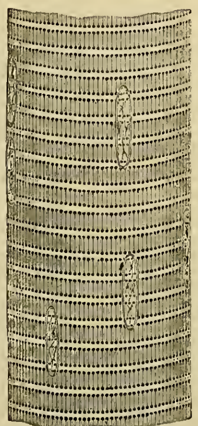
The fibre is represented at a place where the muscular substance has become ruptured and has shrunk away, leaving the sarcolemma (with a nucleus adhering to it) clear. The fibre had been treated with serum acidulated with acetic acid.

as may be seen by altering the focus of the microscope, throughout its substance also. In a moderately extended fibre about eight or nine dark and as many light bands may be counted in the length of $\frac{1}{1000}$ of an inch, which would give about $\frac{1}{17000}$ inch as the breadth of each. But whilst this may be assigned as their usual breadth in human muscle, they are in different parts found to be much narrower, so that not unfrequently there are twice as many in the space mentioned. This closer approximation may generally be noticed in thicker and apparently contracted parts of the fibre. The cross-striped appearance, which is very characteristic, is found in all the skeletal muscles ; but it is not altogether confined

to them, for it is seen in the fibres of the heart, and striped fibres are also found in some other viscera, such as the pharynx and upper part of the gullet.

When the muscular fibres are deeply focussed, the appearance of the striæ becomes somewhat altered, and a fine line, often dotted, is seen passing across the middle of each light band, (see fig. 328). This has been termed *Dobie's line* or the *stria of Amici* (*disque mince*, *Zwischenscheibe*), and it has been supposed to represent a membrane stretching across the fibre and attached at the surface to the sarcolemma (see below). The line is, however, not visible in the most superficial planes of the fibre, and although there certainly are membranes crossing the fibre at about this situation, they are only seen when the fibre is treated with acids and certain other reagents. There is reason to believe that the appearance of a dotted line in this situation in the fresh fibre is due to the peculiar optical conditions of the tissue.

A fine clear line is sometimes to be seen in the middle of each dark band. This was first noticed by Hensen, and named the *line or disk of Hensen*.



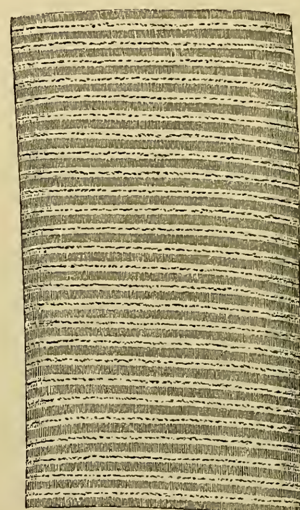


Fig. 327.—Muscular fibre of a mammal examined fresh in serum, highly magnified. (E. A. S.)

This figure was drawn with the surface layer of muscular substance accurately focussed, the lateral portions having been added by gradually sinking the focus.

The nuclei are seen on the flat at the surface of the fibre, and in profile at the edges.

Fig. 328.—Portion of a human muscular fibre showing Dobie's line in the middle of the clear band. (Sharpey.)

The proper substance of the fibre presents, besides the transverse bands, an appearance of longitudinal striation. On separating the fibre with needles, especially after hardening in alcohol, it may be broken up longitudinally into fine longitudinal elements, of a rounded or angular section, which run from end to end of the fibre; these may be conveniently termed *muscle-columns* (Kölliker) or *sarcostyles*.[1] Each sarcostyle appears to consist of a row of elongated prismatic particles with clear intervals. These particles may be termed *sarcous elements* (Bowman). The sarcostyles are united into the fibre by a variable amount of intercolumnar substance to which the name *sarcoplasm* has been given (Rollett). In some muscles the sarcostyles can be made out to be longitudinally striated, an appearance which has led some authors to believe that they are composed of still finer elements or fibrils, a term which has also been employed to denote the muscle-columns themselves.

Under certain circumstances the fibres show a tendency to cleave across in a direction parallel to the bands, and even to break up into transverse plates or

[1] σαρξ, muscle; στῦλος, a column.

disks, which are formed by the lateral cohesion of the sarcous elements of adjacent sarcostyles (fig. 329). To make up such a disk, therefore, every sarcostyle contributes a particle, which coheres with its neighbours on each side, and this with perfect regularity.

From a consideration of these facts Bowman was led to conclude the sub-division of a fibre into "fibrils" (sarcostyles) to be merely a phenomenon of the same kind as the separation into disks, only of more common occurrence, the cleavage in the latter case taking place longitudinally instead of transversely; accordingly, he came to the conclusion that the "fibrillæ" (sarcostyles) have no existence as such in the fibre, any more than the disks; but that both the one and the other owe their origin to the regular arrangement of the particles of the fibre (sarcous elements) longitudinally and transversely, whereby, on the application of a severing force, it cleaves in the one or in the other direction. That this conclusion was erroneous, however, is shown by the fact that a fibre can be split into longitudinal elements after death even without the action of any reagents, but never into disks; and also by the circumstance that in certain muscular fibres (those which move the wings of many insects) a separation into longitudinal elements (sarcostyles) can be seen to preexist even in the living and contractile condition of the fibre. Moreover, in these muscles, in consequence of the large amount of interstitial substance between the sarcostyles, the whole of a fibre never cleaves across into disks.

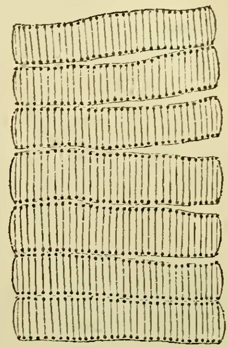


Fig. 329.—Muscular fibre from the leg of a beetle, treated with dilute acid, showing a tendency to break across into disks. (E. A. S.)

The sarcoplasm is in the form of fine longitudinal lines with dot-like enlargements. The ordinary cross-stripes of the tissue are not seen.

If a transverse section of a muscular fibre, or the surface of a separated disk (fig. 330 A), is examined with a high power, it appears to be marked out into small polygonal areas separated by fine lines which, in acid preparations, have the

A B C

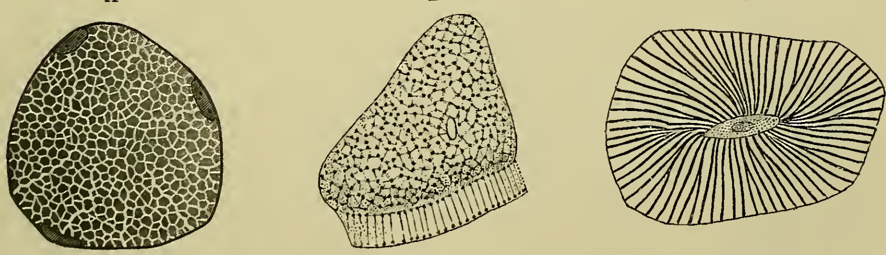


Fig. 330.—Transverse sections of muscle fibres. (E. A. S.)

A.—Transverse section of a mammalian muscular fibre showing Cohnheim's areas. Alcohol preparation. Three nuclei are visible under the sarcolemma.

B.—An isolated disk of leg-muscle of a beetle treated with dilute acid.

The disk is seen partly on the flat, partly in profile, and exhibits the net-like appearance of the sarcoplasm in the transverse section of the fibre: the meshes represent the areas of Cohnheim.

C.—Transverse section of muscular fibre of leg of wasp, showing a radial disposition of the sarcoplasm. Acid preparation.

appearance of a network (fig. 330, B). These areas represent sections of the muscle-columns; they are known as *Cohnheim's areas*, and the lines between them represent the intercolumnar substance or sarcoplasm. The network is coarser near the surfaces of such a disk, because, as will immediately be explained, the sarcoplasm is increased in amount at regular intervals, corresponding with the bright striæ; by alteration of the focus, however, a fine network can be made out through the whole thickness of the disk.

Although such a network as the one which is shown in fig. 330, B, with polygonal meshes, is characteristic of the transverse section of the muscular fibres of vertebrates and of those of some insects, the fibres of many insects have the appearance in transverse section which is shown in fig. 330, C, in which the lines of the apparent network, *i.e.*, of the sarcoplasm, are disposed radially, and the muscle-columns also therefore have a radial disposition and a flattened shape. They are generally, however, subdivided by econdary septa of sarcoplasm (not shown in the figure).

When a muscular fibre is examined in the fresh condition in serum, fine longitudinal lines are seen, as before mentioned, running through the cross striæ (see figs. 327, 331). Under favourable conditions, and especially after the action of weak acid, which swells the muscular substance and renders it clearer and more

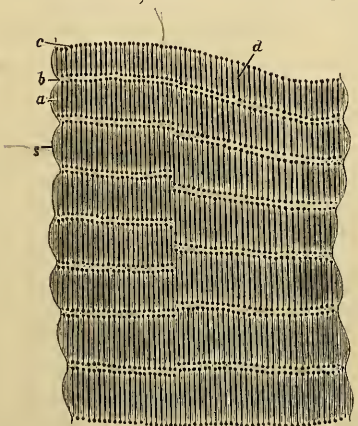


Fig. 331.—Living leg-muscle of water-beetle (dytiscus marginalis). Highly magnified. (E. A. S.)

s, sarcolemma ; *a*, dim stripe ; *b*, bright stripe ; *c*, row of dots in bright stripe, which are enlargements or thickenings on the longitudinal septa of sarcoplasm. These septa are represented by the longitudinal lines, *d*. The continuity of these lines through the bright stripe is difficult to see in the fresh fibre, but after treatment with acid it becomes quite distinct.

transparent, these lines can be traced from end to end of the fibre between the muscle-columns (fig. 332). By careful focussing it can be made out that the lines are really the optical section of the planes of separation between the sarcostyles, that is to say, they are the optical effect of the intro-columnar substance or sarcoplasm. The sarcoplasm, then, has in transverse section of the fibre, the appearance of a network ; in longitudinal optical section the appearance of fine parallel lines ; both these appearances are exhibited in the disk shown in fig. 330, B. It may easily be understood how these two effects would be produced by the presence of a small amount of interstitial substance lying between closely packed prismatic columns.

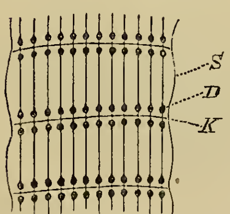


Fig. 332. — Muscular fibre of an insect's leg after short treatment with dilute formic acid. (E. A. S.).

S, Sarcolemma ; *D*, dot-like enlargement of sarcoplasm ; *K*, Krause's membrane.

In most muscular fibres the sarcoplasm further exhibits a peculiarity of arrangement which has a very characteristic influence upon the optical appearance of the fibre. As is shown in the longitudinal view of the fresh muscle (figs. 327, 331), and still more strikingly in the longitudinal view of the muscle which has been treated with acid (figs. 329, 332), the lines which represent the intercolumnar sarcoplasm exhibit enlargements at regular intervals upon their course. These enlargements lie in the bright cross striæ, either near its junction with the dim cross-striæ as shown in figs. 327, 331, or in its middle : in the former case the enlargements form a double row in each bright stria, in the latter case they may be blended into a single row (as in fig. 340). In the longitudinal optical section these enlargements of sarcoplasm have the appearance of dots upon the fine longitudinal lines which run through the muscle : in the more extended fibres or parts of a fibre, these dots are in double rows, in less extended parts they are thicker and blend together in the middle of the bright stria ; this difference is well exhibited in fig. 339 at the parts marked R and I respectively.

The dots of the longitudinal view correspond to the coarser transverse networks which are seen near the surface of the separated disks (fig. 330, B), while the fine lines

of the longitudinal view correspond to the more delicate network seen in other and deeper planes of the disks. It is also clear from what has been said that these rectilinear appearances do not denote the presence of a network of filaments, but are the optical effect of septa separating the muscle-columns, which septa, at the level of the apparent dots, are thickened by the accumulation of a larger amount of sarcoplasm.

In muscular fibres which have been treated first with acid and afterwards with chloride of gold, and which have been placed in formic acid for twenty-four hours, or until the gold has become reduced in the tissue, the sarcoplasm becomes stained of a dark violet colour, while all the rest of the muscular substance remains unstained. The reticular appearances are thereby rendered very distinct, and they have led many histologists to believe that the muscle-substance consists of a contractile *reticulum* composed of longitudinal filaments and transverse networks, and enclosing in its meshes a non-contractile fluid substance (*enchylema*, Carnoy), which is continuous in every direction in the fibre. But it can be proved, as will be seen immediately when the structure of the wing-muscles of insects is considered, that the inter-reticular substance (*i.e.*, the substance forming the muscle-columns) is undoubtedly the contractile part of the muscle, and that the apparent reticulum or sarcoplasm is not contractile. Moreover, careful observation with the highest powers distinctly shows that the filaments of the reticulum are actually septa which subdivide the fibre into longitudinal elements.

Structure of the wing-muscles of insects.—The wing-muscles of insects may be looked upon as furnishing the key to the proper understanding of the

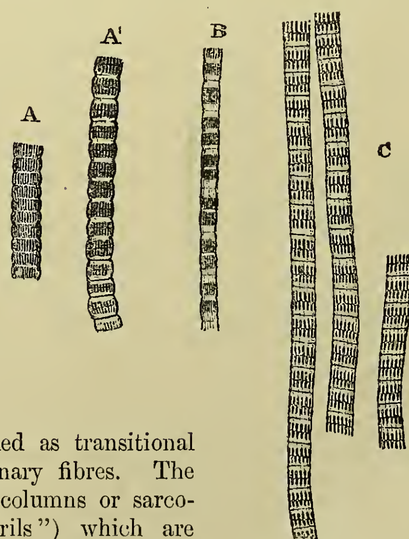


Fig. 333.—Sarcostyles of the wing-muscles of a wasp. Highly magnified. (E. A. S.)

A, A′, sarcostyles showing degrees of retraction (? contraction).
B, a sarcostyle extended, with the sarcous elements separated into two parts.
C, three sarcostyles moderately extended. The structure of the sarcous elements is shown semidiagrammatically in these.

structure of muscle. Although often regarded as a contractile tissue *sui generis* they in fact agree in all essential particulars of structure with the ordinary muscles. Moreover, in some insects they are replaced by muscles of the ordinary type, and in others muscular fibres occur which may be regarded as transitional forms between the wing-fibres and ordinary fibres. The wing-fibres are large bundles of muscle-columns or sarcostyles (often spoken of as "wing-fibrils") which are imbedded in a considerable amount of sarcoplasm containing peculiar granules, the whole being usually enclosed within a sarcolemma (figs. 333, 334). The nuclei of the fibre are scattered here and there in the sarcoplasm, and this has all the appearance and many of the chemical characters of cell-protoplasm. Amongst these characters is that of staining darkly with chloride of gold, in which respect the sarcoplasm of the wing-muscles exactly resembles the apparent reticulum of ordinary muscles. The main difference is one of amount, the quantity of sarcoplasm in the wing-muscles being relatively far greater (fig. 334) than in the ordinary muscles.

When a living wing-fibre is broken up with needles in a small drop of white of egg, the sarcostyles become easily separated from the sarcoplasm which surrounds

them, and they can then be studied independently of that substance. And in the first place it may be mentioned that they can, under these circumstances, be seen to contract, whereas the sarcoplasm gives no sign of contractility: they therefore

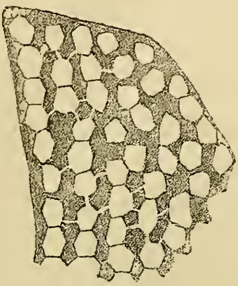


Fig. 334.—Transverse section of part of a wing-fibre of an insect showing the sarcostyles surrounded by sarcoplasm. (E. A. S.) $\frac{1000}{1}$

The muscle was treated with chloride of gold and acid, so that the sarcoplasm has become stained, the sarcostyles being left colourless.

form the active portion of the fibre. The intimate structure of the sarcostyles can be advantageously investigated in such isolated elements, and this both in the living condition and under the influence of reagents. In the living condition they show, as in the ordinary muscles, alternations of bright and dim striæ. Each bright stria is bisected by a line which is the optical section of a transverse membrane (*membrane of Krause*). These membranes thus divide the fibre into a series of segments, which may be termed *sarcomeres*. In alcohol-hardened muscle each sarcomere can be seen to contain (1) in the middle a strongly refracting disk-like sarcous element; (2) at either end (next the membrane of Krause) a clear interval occupied by hyaline substance. With high powers the sarcous element may be made out to be composed of a *sarcous substance,* which stains with hæmatoxylin, and is pierced by short tubular canals which extend from the clear interval as far as the middle of the disk; these canals give it a longitudinally striated appearance. Fine longitudinal striæ which appear to be due to delicate extensions of the sarcous

Fig. 335.—Disk-like sarcous element of wing-muscle showing its tubular structure. Highly magnified. (E. A. S.) From a photograph. $\frac{2300}{1}$

A, Profile view. B, Viewed in optical transverse section.

substance (perhaps delicate septa), may also, under favourable circumstances be seen traversing the clear intervals. If the sarcostyle is extended, the sarcous elements tend to separate into two parts, with an interval between them (fig. 333, B); this median clear interval corresponds with the line of Hensen (p. 288).[1] Conversely, if the muscle is retracted (or contracted) the sarcous elements tend to encroach on the clear intervals and approach the membranes of Krause; and at the same time they become swollen, so that the sarcomeres are bulged out at their middle and contracted at their ends. The sarcostyles thus become moniliform, and in fresh and unstained fibres the effect of this form upon the light transmitted through the muscle is such that the swollen part looks comparatively clear, while the constricted part has a dark appearance; and since this constricted part corresponds with the bright stria of the extended muscle, the striæ appear to have become reversed during contraction. In a stained fibre, however, it is easy to see that no such reversal takes place in contraction (fig. 333, A, A′).

Comparison of the structure of muscle with that of amœboid protoplasm.—If we compare the structure of the muscle-columns as shown in the wing-muscles with that of amœboid protoplasm, we find many points of coincidence. Both are composed of two kinds of substance, viz., a porous substance or spongioplasm which stains with hæmatoxylin and similar reagents, and a clear matter or hyaloplasm which remains unstained. In both cases the process of contraction is accompanied by a flowing of the hyaloplasm into the pores or meshes

[1] With still further extension, each sarcous element may separate into four parts, in which case the two parts nearest the transverse membrane have been termed the *accessory disks.*

of the spongioplasm; while on the other hand, when the contraction passes off, the hyaloplasm tends to pass out from the pores or meshes of the spongioplasm, and produces in the one case extension of the muscle-fibre, in the other the throwing out of pseudopodia. In short the poriferous substance of the sarcous element corresponds with the spongioplasmic "œcoid" of the amœboid cell, whilst the clear substance which flows in and out of the pores represents the hyaloplasmic "zooid" (see p. 178).

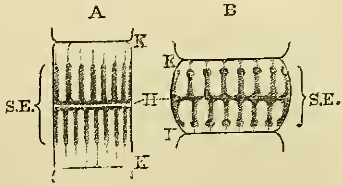


Fig. 336.—Diagram of a sarcomere in a moderately extended condition A, and in a contracted condition B. (E. A. S.)

K, K, Membranes of Krause; H, plane of Hensen; S.E., poriferous sarcous element.

Comparison of the ordinary muscles of insects and vertebrates with the wing-muscles of insects.—The differences of structure between the ordinary muscles and the muscular fibres which move the wings of insects, are of no great importance, being differences of degree only. Thus the sarcoplasm is in relatively small amount in the ordinary muscles, and generally has the regular enlargements which appear as dots or transverse networks according to the point from which they are viewed, these enlargements being absent in the wing-fibres; moreover, the sarcostyles or muscle-columns, probably on account of the smaller amount of sarcoplasm, are less easily isolated. But, like the sarcostyles of the wing-muscles, they are divided into segments or sarcomeres, at regular intervals, corresponding with the middle of the bright striæ, by transverse membranes (membranes of Krause), which can be brought distinctly

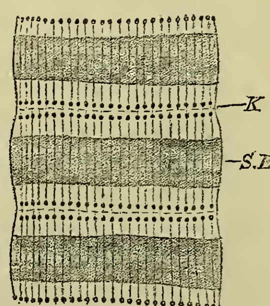


Fig. 337.—Part of a muscular fibre of an insect fixed with alcohol and afterwards stained. (E. A. S.)

The rows of sarcous elements which form the dark stripes are stained (S.E.); the sarcoplasm has the usual appearance of longitudinal lines and dots. The lines produced by the juxtaposed membranes of Krause are just visible (K.).

into view on the addition of dilute acid to the fresh or alcohol-fixed muscle (fig. 332, K). Each sarcomere contains a sarcous element, with hyaline substance between the sarcous element and the membrane of Krause at either end of the segment: the middle of the sarcous element when the muscular fibre is extended shows a line, as in the wing-element,—the band of Hensen.

As in the wing-sarcostyles, the proportionate amounts of the sarcomere occupied respectively by the sarcous element and the clear intervals vary greatly, especially according to the condition of extension or retraction of the muscle. In retracted or contracted fibres the sarcous elements bulge out and approach the transverse membranes, and the clear intervals diminish proportionately, their fluid being imbibed by the sarcous element, while in extended fibres the sarcous elements become removed from the transverse membranes and narrowed, and the clear intervals become *pari passu* longer.

It is said that the ends of the sarcous element may in extended fibres become detached and form accessory disks lying in the clear interval. It is certain, however, that the structures which have often been described as accessory disks in these muscles are merely the sarcoplasmic enlargements which appear as dotted lines.

Effect of the sarcoplasmic accumulations upon the cross-striation of the ordinary muscles.—An important influence upon the optical appearances of the ordinary muscular fibres is exerted by the sarcoplasmic accumulations (transverse networks). These lie, as we have seen, in the region of the bright stripe (clear

interval of the sarcomere), and have in optical section the appearance of rows of dark-looking dots. When these dots are carefully regarded they seem each to be surrounded by a bright halo (figs. 331, 339, R), which is apparently due to the manner in which they reflect the light which is transmitted through the muscle, much in the same way as an oil-globule or an albuminous granule, when viewed in water under a

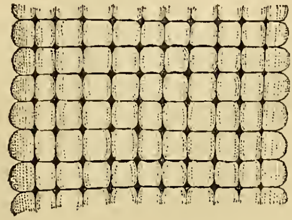


Fig. 338.—Part of a contracted fibre of insect muscle (leg) treated with vinegar. (E. A. S.)

The moniliform appearance of the sarcostyles and the accumulations of the sarcoplasm opposite their constrictions are well seen. The ordinary cross-striation is not visible.

high power of the microscope, appears when it is exactly focussed, to be surrounded by a bright area.[1] Since each dot is encircled by a bright halo, and the dots are arranged in regular rows, the haloes become blended into a stripe, which is much brighter than the rest of the muscle-substance. This is in fact the chief cause of the very bright appearance of the clear bands of the fresh muscle. These clear bands, however, about correspond in level with

R

I

C

I

R

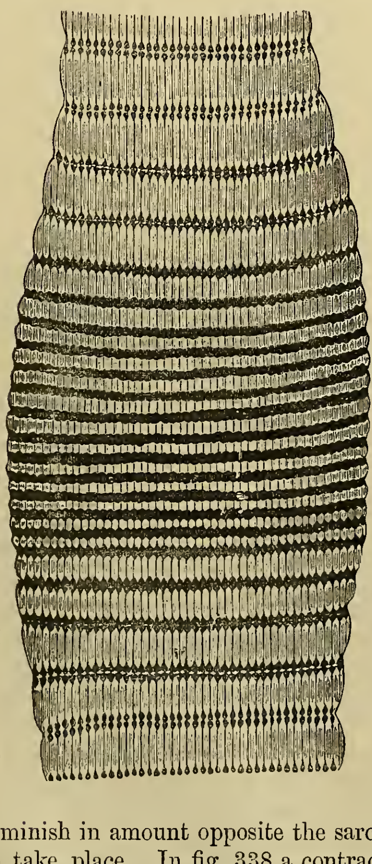


Fig. 339.—Wave of contraction passing over a muscular fibre of dytiscus. Very highly magnified. (E. A. S.)

R, R, portions of the fibre at rest; C, contracted part: I, I, intermediate condition.

the hyaline substance of the sarcomeres as seen in stained alcohol-preparations, so that their relatively bright appearance in the fresh muscle, as compared with the dim band or row of sarcous elements, is not entirely produced by the light-effect above mentioned, although it is greatly enhanced thereby.

Changes in contraction.—When these muscles contract the sarcous elements, as in the wing-muscles, become bulged out and shortened, while the fluid of the clear intervals becomes relatively diminished in amount. The ends of the sarcomeres are thereby contracted opposite the membranes of Krause, and the sarcostyles become moniliform (fig. 338).

This alteration in shape of the sarcostyles necessarily affects the sarcoplasm which lies in their interstices, which must become squeezed out of the parts which are opposite the bulgings of the sarcostyles and into the parts which are opposite their constrictions. In other words, the sarcoplasm must accumulate in greater quantity opposite the clear bands and the membranes of Krause, and must diminish in amount opposite the sarcous elements. This is, in fact, what can be seen to take place. In fig. 338 a contracted portion of muscle in which the sarcoplasm has been rendered evident by acid is represented, and it is seen that the sarcoplasm

[1] It is in fact this action of the dots upon the light which tends to obscure the continuity of the longitudinal lines of the sarcoplasm in the fresh condition, so that in this condition it may be difficult or impossible to make out that continuity (see fig. 331).

is accumulated opposite the transverse membranes where the sarcostyles are relatively contracted.

In the living muscle also this change in the position of the sarcoplasm during contraction can, with care, be observed to take place (fig. 339). In this case, also, as in the wing-sarcostyles, the moniliform shape of the muscle-columns tends to cause the constricted parts to appear dark, the bulged parts light in comparison, so that the effect of reversal of the striæ is obtained. But in the ordinary muscles this effect is materially increased, and the contrast between the dark and light striæ of the contracted muscle is greatly enhanced by the effect of the sarcoplasmic accumulations opposite the constrictions. For in the first place these themselves tend to produce the appearance of dark lines or planes passing across the fibre, and, besides this, the light-reflexions from their surfaces cause the muscular substance between these planes to appear much brighter than would otherwise be the case.

In alcohol-preparations (both of the wing-muscles and of the ordinary muscles) in which the sarcous elements have been subsequently stained, there is no appearance of reversal of striation ; the darkly coloured sarcous element always occupies the central or bulged part of the sarcomere, and the unstained substance of the clear intervals the constricted parts of the sarcostyles.

Appearances of muscle under polarised light.—It was noticed by Boeck that, like some of the other tissues, muscle is doubly refracting (anisotropous). Brücke however was the first to point out that the fibre is not composed entirely of anisotropous substance, but that there is in addition a certain amount of singly refracting or isotropous material. Since the important researches of the last-named author form the basis of our knowledge of this subject, a short account will be given of them here.

In the first place Brücke distinguishes between the appearances presented by living muscle examined in its own plasma and those of dead and hardened muscle examined in glycerine or Canada balsam. Under the latter conditions, although a considerable variation is noticeable in the relative amount of anisotropous substance, nevertheless the two substances invariably take the form of alternating bands, dark and light, crossing the fibre and apparently corresponding in position with the light and dark stripes of the fibre as seen under ordinary light.

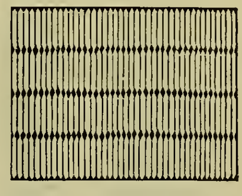


Fig. 340.—Living muscle of a water-beetle examined in polarized light with crossed Nichol's prisms. (Brücke.)

It is quite otherwise with living muscle. In this almost the whole of the fibre may look doubly refractile, the isotropous substance occurring only as fine transverse lines, or as rows of rhomboidal dots which are united to one another across the anisotropous substance by fine longitudinal lines. This account is illustrated by fig. 340, which is copied from Brücke. If this figure be compared with fig. 331, or with the parts marked I of fig. 339, which represent the living muscle of a water-beetle under ordinary light, it is obvious that the rhomboid points and longitudinal lines of the one correspond to the sarcoplasmic lines and transverse networks of the other. The sarcoplasm therefore is singly refracting, whereas the substance of the muscle-columns or sarcostyles is, in great part at least, doubly refracting. Brücke's account of the appearance of living muscle under polarised light seems to have been chiefly founded upon fibres which are not extended, and in which therefore the sarcous elements occupy by far the larger part of the sarcomere. In extended fibres or parts of fibres, especially those which have been fixed by alcohol and mounted in Canada balsam, the fibre appears when examined between crossed Nichol's prisms to be marked by alternating broad bars of light (anisotropous) and dark (isotropous) substance, the former corresponding in position to the sarcous elements, the latter to the clear intervals of the sarcostyles. In the wing-muscles also the sarcous elements appear bright and the clear intervals, including Krause's membrane, are dark with crossed Nichols. In less extended parts of the fibre, the dark or isotropous bands become relatively narrower until in the contracted parts they are reduced to comparatively narrow bands, with relatively broad bright (anisotropous) intervals (fig. 341). There is however no reversal of the bands, a fact of some significance as indicating that the reversal which *appears* to occur when the fibre is examined by ordinary light is really, as has been already explained, merely an optical effect, and is not caused by any actual change in the relative position within the sarcomere of the substance of the sarcous elements and the clear intervals (see below, Theory of Merkel). The result therefore of the examination of muscle under polarised light is confirmatory of the deductions

which may be drawn regarding its structure and the changes which occur in contraction, from the appearance of stained preparations, and tends to show that the chromatic substance of the sarcostyles—the substance which forms the sarcous elements—is anisotropous, while the substance or fluid of the clear intervals as well as the sarcoplasm is isotropous. In muscles which have been treated with acid and in which the sarcous elements are destroyed all appearance of double refraction is found to have disappeared.

It has been shown by Ranvier that the appearance of a tissue under polarised light affords, when taken by itself, no guide to its structure. For the same tissue or part of a tissue may appear either light or dark between crossed Nichols, according to the direction and character of the "stress" to which it may have been exposed, in the same way that a film of indiarubber, which is normally isotropous, becomes anisotropous when stretched. Looked at however in conjunction with other facts, and especially with the results of methods of staining, the appearance under polarised light may afford important confirmation, or the reverse, of the deductions which may be drawn regarding structure by the employment of these methods : this is exhibited by the observations upon muscle which have been above detailed.

Brücke has applied the theory of Bartholin (invented to explain the phenomena of double refraction in crystals of Iceland spar, and which supposes that those crystals are compounded

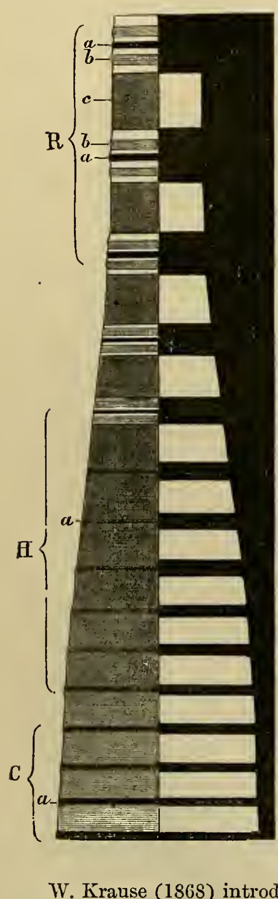


Fig. 341.—Muscular fibre of an insect, exhibiting part of a so-called "fixed wave of contraction." (Engelmann.)

The right half of the figure shows the effect produced by the same fibre when examined under polarised light, the rows of sarcous elements then appearing light on the dark field caused by the crossed Nichols' prisms.

R, part at rest and extended ; H, part passing into contraction ; C, contracted part. *a*, intermediate disk ; *b*, accessory disk ; *c*, principal disk.

of minute doubly refracting particles (disdiaclasts)), to the doubly refracting substance of muscle, and has applied the same name (*disdiaclasts*) to the particles of which he supposes that substance to be composed, and which would appear to act upon the light like positive, uniaxial, doubly refracting crystals. Under certain circumstances, as after the action of water or salt solution, the muscular substance is apt to break down into a cloud of fine doubly refracting particles which are either themselves the disdiaclasts or represent groups of them.

Historical.—Until Bowman published, in the Philosophical Transactions for 1840, his important work on the structure of muscle, the whole subject was exceedingly obscure. The view which Bowman took of the constitution of muscular substance, namely, that it is composed of a series of particles joined together closely side by side into disks, and less intimately united end to end into "fibrils," long occupied a dominant position in this branch of histology. Kölliker however (1851), laying stress upon the fact that the muscular substance is much more apt to break up into "fibrils" than into disks, looked upon the appearance of the latter as altogether secondary, and regarded the "fibrils" as the actual elements of the muscle, the alternate dark and light portions in the course of each fibril being of essentially the same nature, although differing somewhat in their optical properties. Afterwards (1867), recognising that the so-called fibrils might be composed of finer elements, or ultimate fibrils, Kölliker was led to term the structures formerly known as fibrils "muscle-columns," the areas of Cohnheim representing the transverse sections of those columns. The fibrillar constitution of muscle has also been consistently urged by G. Wagener.

W. Krause (1868) introduced an entirely new idea into the conception of the subject, by looking upon the intermediate line in the light stripe as a continuous disk or membrane, united laterally to the sarcolemma, and thus dividing the whole fibre into a series of flat compartments, these being again subdivided longitudinally by partitions (seen on transverse section as the clear lines bounding Cohnheim's areas), so that little cases (*Muskel-kästchen*) are thus formed (fig. 342, A). Each such case contains, according to Krause, a portion of the dark disk (muscle-prism) in its middle part, and portions of the light disks (fluid) at either end, and Krause supposed that in contraction this fluid changes its situation, becoming shifted to the periphery of the dark substance, and that in this way the muscle is diminished in length, and

proportionately increased in breadth (fig. 342, B). Subsequently, however, recognising the existence of longitudinal elements within the muscle-prism, Krause described the fluid as passing between these and separating them more from one another during contraction (C).

About the same time (1868), Hensen described the stripe which bears his name.

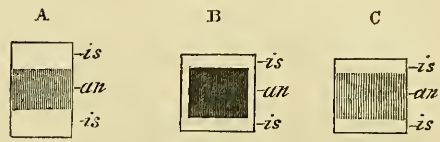


Fig. 342.—Diagrammatic representation of a muscle-case under a very high magnifying power. (W. Krause.)

A, at rest; B, condition in contraction, former view; C, condition in contraction, present view. *an*, muscle-prism, consisting of a bundle of muscle-rods; *is*, fluid isotropous substance.

The next prominent writer upon the subject was Merkel (1872), who described the transverse membranes of Krause as being double, and who corroborated Hensen's description of the existence of a thin line or disk in the middle of the dark stria. But the most important difference in Merkel's account occurs in his description of the process of contraction. According to Merkel, the anisotropous substance of the dark stria first of all becomes diffused over the whole muscle compartment, so that the fibre acquires a homogeneous appearance, and then at a later stage becomes accumulated against the transverse membranes, while the isotropous substance on the other hand is accumulated on either side of Hensen's disk, so that the position of the two substances is thus reversed. In a subsequent communication (1881) a somewhat modified view of the changes in contraction was taken by Merkel.

Merkel was followed by Engelmann (1873), according to whose description, a muscular fibre consists of a succession of superimposed parts or compartments, which are partitioned off from one another by thin disks or membranes—Krause's membranes or intermediate disks (fig. 341, *a*, *a*). Within each compartment thus marked off is a series of disks, varying in their refractive power and in their action upon polarised light, as follows :—Next to an intermediate disk comes a layer of isotropous clear substance, within which may be distinguished a thin disk of dark substance (*b*), having in ordinary muscles the appearance of a line of dots, the accessory disk (granule-layer of Flögel); then comes a broad disk of anisotropous substance (principal disk, *c*), occupying the greater portion of the muscle-compartment, and sometimes bisected by a narrow pale band, which lies exactly in the middle of the compartment, and is distinguished as the middle disk or disk of Hensen (not seen in the figure). Beyond the broad anisotropous disk come in inverse succession isotropous substance with accessory disk, and intermediate disk, and so on in the next compartment.

When contraction is about to supervene in any part of a muscular fibre, the changes, which according to Engelmann may be observed, are the following :—While the intermediate disks approach one another, the successive disks within each muscle-compartment become less distinct, and the fibre loses in great measure at the part in question (that namely in which the contraction is beginning), its striated appearance. The stage in question was accordingly termed by Engelmann the homogeneous stage (fig. 341, H.). As the contraction progresses, transverse striæ again make their appearance, in consequence of the gradual darkening of the accessory disks and concomitant clearing up of the principal disk, so that now each intermediate disk with its juxtaposed accessory disk forms a distinct dark isotropous band, these alternating with the narrowed and now bright-looking principal disks of anisotropous substance (fig. 341, C.) The reversal of the striæ in contracting muscle is ascribed by Engelmann to changes in refrangibility in the several substances which compose the disks of the muscle-compartment. accompanied by an increase in the volume of the principal disk at the expense of the isotropous substance.

Both Merkel and Englemann attach considerable importance to the occurrence of the intermediate stage, in which the striæ become indistinct; but it is probable that the homogeneous appearance of that part of the fibre which is passing into or out of full contraction is due to a shifting of the longitudinal elements of the muscle, owing to their being unequally pulled upon by the more completely contracted part. A similar mechanical shifting of the muscle-columns, accompanied by disappearance of distinct transverse striation, is often produced in teasing the tissue. Moreover the so-called homogeneous stage is often not observed in contracting muscle. It must therefore be regarded as an adventitious appearance.

Heitzmann (in 1873) seems to have been the first to notice the reticular appearances of muscle which had been treated with gold and acid, but these appearances were first fully described by G. Retzius in 1881, who showed that the dots or enlargements upon the longitudinal lines of the muscular substance are actually only the optical sections of the fibres of transverse networks, which Retzius regarded with great probability, as extending from and continuous with the protoplasm surrounding the nuclei of the muscle fibre.

Carnoy's theory of the constitution of cell protoplasm of a contractile reticulum and enchylema, which was about this time beginning to rise into importance, had a marked influence

upon the following series of researches into the structure of muscle. Various observers (Melland, G. F. Marshall, van Gehuchten and Ramón y Cajal), who during the next five or six years investigated the structure of muscle, mainly with the aid of acid and gold preparations, have regarded the appearances of these preparations as proving the existence of a similar reticulum in muscle, and have concluded that the material in the meshes of the supposed reticulum, that is to say the whole of the muscle-columns, must represent the enchylema of protoplasm. The breaking up of the so-called inter-reticular substance into muscle-columns is regarded as purely artificial.

Although the above view of muscle-structure obtained for a short time some adherence amongst histologists, and has not even at the present time been given up by all its original supporters, it must certainly be relinquished as being inconsistent with the known facts of muscle-structure. The researches of Rollett, which were published in 1885 and 1886, showed any such view to be untenable, and brought the matter back to the former standpoint. The results of these researches tended to demonstrate that the filaments of the so-called "reticulum" of the above-mentioned authors are neither more nor less than the septa of sarcoplasm which intervenes between columns of the muscle-substance: that these columns pre-exist in muscle, and are the actual contractile elements of the muscle; and that the sarcoplasm between them is a passive material, and may represent the undifferentiated remains of the protoplasm of the original cell from which the muscular fibre has been developed.

The account in the text is derived from a re-investigation of the structure of muscle, and especially of the muscles of insects, prepared by various methods and photographed with the aid of Zeiss' 2 mm. homogeneous apochromatic objective. It differs materially from that in the last edition of this work, which was based mainly upon investigation of living muscular tissue only. The description of the actual appearances of living muscle still however stands good, and has been retained in this edition.

Muscle-nuclei (muscle-corpuscles).—In connection with the cross-striated substance a number of clear oval nuclei are found in the fibres. In mammalian muscles they lie mostly upon the inner surface of the sarcolemma (figs. 326, 330, A), but in frogs they are distributed through the substance of the fibre, and in many insects they form a longitudinal series situated in the middle of the fibre. Associated with and surrounding them there is sometimes, but not always, a certain amount of granular protoplasm. In the unaltered condition the nuclei are not easily seen, but they are made conspicuous by the addition of acid. They may contain a network of chromoplasm, in which one or two nucleoli are generally visible, but frequently the chromatin of the nucleus is in the form of a spiral filament.

Variations of structure in different muscles, correlated with differences of function.—In the rabbit, as especially pointed out by Ranvier and Krause, certain of the voluntary muscles present differences in appearance and mode of action from the rest. Thus while most of the voluntary muscles have a pale aspect and contract energetically when stimulated, some such as the semi-tendinosus and the soleus in the lower limb, are at once distinguished by their deeper colour as well as by their slow and prolonged contraction when stimulated. When subjected to microscopical examination it is found that in the red muscle the fibres are more distinctly striated longitudinally and the transverse striæ are much more irregular than usual. The muscular fibres are generally finer (thinner) than those of the ordinary muscles, and appear to have a larger amount of sarcoplasm. The nuclei are more numerous and are not confined to the inner surface of the sarcolemma, but occur scattered in the thickness of the fibre as well. There is also a difference in the blood-supply of the two kinds of muscle, to be afterwards alluded to.

A similar difference between red and pale muscles may be also seen in the rays amongst fishes. In other animals the distinction is not found as regards whole muscles although it may affect individual fibres of a muscle. This is the case, according to Klein, in the diaphragm, in which in many of the fibres there are numerous nuclei, and these are embedded in protoplasm, which forms an almost continuous layer underneath the sarcolemma. The distribution of the two kinds of fibres in different muscles has been recently more especially investigated by Grützner

and others working under his direction, and for the details of these investigations the reader is referred to the papers on this subject which are quoted in the Bibliography at the end of this chapter.

Mode of attachment of muscular fibres: ending of muscle in tendon.—When a muscle ends in a tendon it is found that the muscular fibres either run in the same direction as the tendon-bundles or join with the tendon at an acute angle. In the former case the tendon becomes subdivided, either gradually or suddenly, into as many small bundles as there are fibres in the end of the muscle, and it often seems at first sight as if the tendon-fibres were directly continued into the muscular substance. In reality, however, the fibres of each tendon-bundle end abruptly on reaching the rounded or obliquely truncated extremity of a muscular fibre (fig. 343),

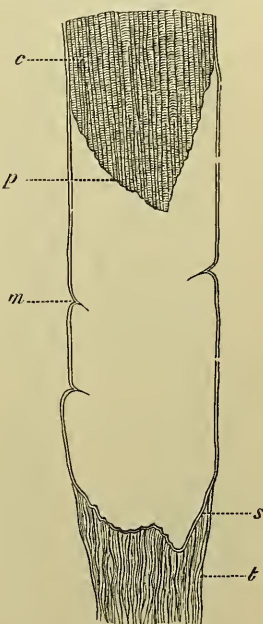


Fig. 343.—Termination of a muscular fibre in tendon. (Ranvier.)

m, sarcolemma ; *s*, the same membrane passing over the end of the fibre ; *p*, extremity of muscular substance, *c*, retracted from the lower end of the sarcolemma-tube ; *t*, tendon-bundle passing to be fixed to the sarcolemma.

and are so intimately united to the prolongation of sarcolemma which covers the extremity, as to render the separation between the two difficult if not impossible (Ranvier). The muscular substance, on the other hand, may readily be caused to retract from the sarcolemma at this point. The areolar tissue which lies between the tendon-bundles, passes between the ends of the muscular fibres and is gradually lost in the interstitial connective tissue of the muscle.

When the direction of the muscular fibres is oblique to that of the tendon, the connection takes place in a similar way to that above described, but the small tendon-bundles are given off laterally along the course of the tendon, which in these cases is generally prolonged into or over the muscle.

When the muscular fibres divide, each branch of the fibre is described as being directly continuous with a tendon-bundle, or connective tissue bundle, without the intervention of sarcolemma, but it is not improbable that renewed careful investigation might, in this case also, disclose the existence of a thin prolongation of sarcolemma over the divisions.

Blood-vessels.—The blood-vessels of the muscular tissue are very abundant, so that, when they are successfully filled with coloured injection, the fleshy part of the muscle contrasts strongly with its tendons. The arteries, accompanied by their associate veins, enter the muscle at various points, and divide into branches : these pass along the fasciculi, crossing over them, and dividing more and more as they get between the finer divisions of the muscle ; at length, penetrating the smallest fasciculi, they end in capillary vessels, which run between the fibres. The vessels are supported in their progress by the sub-divisions of the sheath of the muscle, to which also they supply capillaries. The capillaries destined for the proper tissue of the muscle are extremely small ; they form among the fibres a fine net-work, with narrow oblong meshes (fig. 344), which are stretched out in the direction of the fibres ; in other words, they consist of longitudinal and transverse vessels, the former running parallel with the muscular fibres, and lying in the angular intervals between them,—the latter, which are much shorter, crossing between the longitudinal ones, and passing over or under the intervening fibres.

In the deeper coloured muscular fibres of those animals which, like the rabbit, possess two kinds of voluntary muscles, the transverse loops of the capillary network are dilated far beyond the size of the ordinary capillaries.

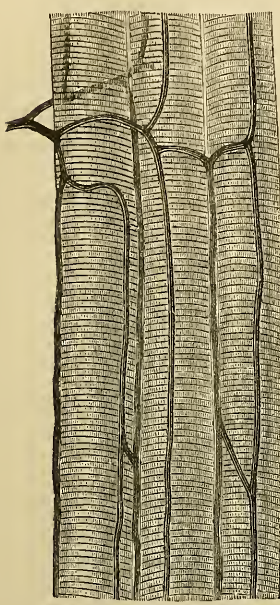


Fig. 344. — CAPILLARY VESSELS OF MUSCLE, MODERATELY MAGNIFIED. (E. A. S.)

The number of capillaries in a given space of a muscle, or their degree of closeness is partly regulated by the size of the fibres; and accordingly in the muscles of different animals it is found that, when the fibres are small, the vessels are numerous and form a close network, and *vice versâ*: in other words, the smaller the fibres, the greater is the quantity of blood supplied to the same bulk of muscle. In conformity with this, we see that in birds and mammalia, in which the process of nutrition is active, and where the rapid change requires a copious supply of material, the muscular fibres are smaller and the vessels more numerous than in cold-blooded animals, in which the opposite conditions prevail.

Lymphatics.—So far as is known there are no lymphatic vessels in the voluntary muscles, although there is an abundant supply in their connective tissue sheaths and tendons, and the lymphatic vessels here would seem, as pointed out by Ludwig and Schweigger-Seidel, to serve the purpose of collecting and conveying away the lymph from the muscular substance.

Nerves.—The nerves of a voluntary muscle are of considerable size. Their branches pass between the fasciculi, and repeatedly unite with each other in form of a plexus, which is for the most part confined to a small part of the length of the muscle, or muscular division in which it lies. From one or more of such primary plexuses, nervous twigs proceed, and form finer plexuses composed of slender bundles, each containing not more than two or three dark-bordered nerve-fibres, whence single fibres pass off between the muscular fibres and divide into branches which are finally distributed to the tissue. The mode of final distribution will be described with the general anatomy of the nerves.

DEVELOPMENT OF VOLUNTARY MUSCULAR TISSUE.

Most of the voluntary muscles of the body are developed from a series of portions of mesoblast which are early set aside for this purpose in the embryo and are termed the muscle-plates (*see* Embryology, p. 159). When the muscular fibres are about to be formed the cells become elongated, and their nuclei multiplied so that each cell is converted into a long multi-nucleated protoplasmic fibre. At first the substance of the fibre is not striated but is merely granular in appearance, but presently it becomes longitudinally striated along one side (fig. 345, A), and about the same time a delicate membrane, the sarcolemma, may be discovered bounding the fibre. The longitudinal striation, which is the first indication of the proper muscular substance, extends along the whole length of the fibre, but at first as just intimated affects only a small part of its breadth, the rest being formed by a highly glycogenic protoplasm containing the nuclei. In due time, however, this conversion into the proper muscular substance, further shown by the appearance of cross striæ (fig. 345, B and C), extends round the greater part of the circumference of the fibre, and finally gradually involves its whole thickness, except along the axis, which for some time remains occupied by the nuclei embedded in undifferentiated protoplasm. Eventually, however, the nuclei take up their permanent position.

Schwann considered each fibre to be formed by the linear coalescence of several cells; but the researches of Kölliker, Wilson Fox, and others, tend to establish the

view, originally promulgated by Remak, that the fibres are produced as above described by the elongation of single cells, with differentiation of their contents and multiplication of their nuclei.

Growth.—The muscular fibres, after having acquired their characteristic form and structure, continue to increase in size till the time of birth, and thenceforward up to adult age. In a full-grown fœtus most of them measure twice, and some of

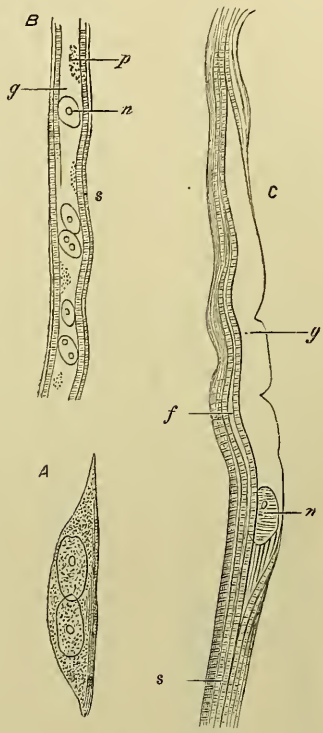


Fig. 345.—Developing muscular fibres. Highly magnified.

A, elongated cell with two nuclei and a striation beginning down one side of the cell (from fœtal sheep, Wilson Fox).

B, from fœtus of 2 months; *p*, granular protoplasm; *g*, glycogenous substance; *n*, nucleus; *s*, commencing sarcolemma, with striated muscular substance developing immediately beneath it.

C, from fœtus of 3 months, displayed so as to show the contractile substance collected at one side of the fibre, and partially enclosing the unaltered substance of the fibre, *g*; *f*, fibrils. B and C from Ranvier.

them three or four times their size at the middle of fœtal life; and in the adult they are about five times as large as at birth. This increase in bulk of the individual fibres would, in a measure, account for the enlargement of the entire muscles.

It is uncertain how far there may be a multiplication or new formation of muscular fibres during the growth of a muscle; but it is probable that during growth at least, if not in adult life, a new formation of fibres within the muscles does occur. The new fibres appear to be in part formed by the longitudinal splitting of the existing fibres, a process which was described by Weissmann, and which seems to be of very general occurrence at a certain period of growth. The splitting is preceded by the multiplication of the muscle-nuclei, which form a longitudinal series in the part which is about to become separated. The bundle of fine muscular fibres is found to be enclosed within a thick connective tissue sheath formed of several layers, continuous with the layers of Henle's sheath of the nerve-fibre, and since these layers are more developed at the point of entrance of the nerve into the bundle than elsewhere, the whole structure has a spindle-shape, and on this account has received the name of *muscle-spindle* (Kühne). The fibres of the muscle-spindle appear gradually to enlarge and eventually to form a bundle of ordinary muscle-fibres. The nerve and nerve-ending must, of course, participate in the cleavage, since each fibre is ultimately found to be furnished with a nerve-ending. But another important mode of new formation is by the transformation of cells (sarcoplasts) which lie between the muscle fibres, and which are presumably undifferentiated cells derived from the original muscle-plate. These cells enlarge and become elongated, and striated muscular substance becomes formed within them usually at one side, and often forming oval masses, which as they grow become longer and more spindle-shaped, the middle part being bulged out and the ends tapering off to fine terminations. At this stage of development the name of muscle-spindle has also been applied to these fibres. The middle bulged part receives a nerve fibre, which is provided with a terminal ramification, as with other muscular fibres, and a multiplication of nuclei, and formation of sarcolemma having already taken place, the development of the fibre may now be looked upon as completed. Such fibres in

various stages of development have been described in muscles at all stages of growth, and also in the adult condition, so that it has been conjectured that new muscular fibres may be formed in this way even after the development of the muscle is completed. Nothing is known of the manner in which absorption of pre-existing fibres is effected to make room for the newly-formed fibres ; if, indeed, such change occurs at all.

According to Mayer, many of the structures which have been described, under the name sarcoplasts and muscle-spindles, as fibres in course of development, are in reality fibres undergoing degeneration. Kerschner, on the other hand, from their relatively large nerve supply, believes the muscle-spindles to be sensory end-organs.

Regeneration.—It was formerly thought that after removal by the knife or by disease striated muscular tissue is not regenerated, but that any breach of continuity which may occur in a muscle is filled up by a growth of connective tissue. It would appear, however, that the breach is, after a certain lapse of time, bridged across by muscular substance, but how the new muscular tissue is formed is not fully understood.

PLAIN OR UNSTRIPED MUSCULAR TISSUE.

This is made up of cells, named *contractile fibre-cells*, which were first distinguished as the true elements of the tissue by Kölliker. The cells may form fibrous bundles, and strata, or may be less regularly arranged, and the tissue occurs either almost pure or mixed with other tissues in varying proportion. The cells are of an elongated fusiform shape (figs. 346 and 347), usually pointed at the ends. They are generally prismatic in transverse section, but are sometimes more flattened. The cells vary greatly in length according to the part or organ in which they are found. Some occur which are cleft or forked at one or both ends. Their substance is finely vacuolated and exhibits also a faint longitudinal fibrillation. It is doubly refracting. Each cell has a nucleus (*a*, *a*), rarely more than one, which is always elongated and either oval or rod-shaped. Towards each end of the nucleus the substance of the cell usually contains a few distinct granules arranged in linear series.

Fig. 346.—Muscular fibre-cells from the muscular coat of the small intestine, highly magnified. (E. A. S.)

A, a complete cell, showing the nucleus with intranuclear network, and the longitudinal fibrillation of the cell-substance, with protoplasm between the fibrils.

B, a cell broken in the process of isolation ; the delicate enveloping membrane projects at the broken end a little beyond the substance of the cell (B is from a drawing by Mr. R. Boxall).

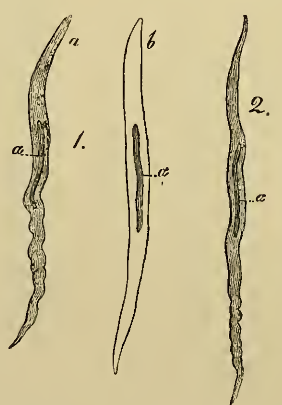


Fig. 347.— Muscular fibre-cells from human arteries, magnified 350 diameters. (Kölliker.)

a, *a*, nucleus ; *b*, a cell treated with acetic acid.

The nucleus shows the usual structure, having an intranuclear network (fig. 346, A). The involuntary fibre-cells possess an exceedingly delicate homogeneous sheath (fig. 346, B), and like the sarcolemma of voluntary muscular fibres, this sheath is apt to be wrinkled when the fibre is

contracted, so that an indistinct appearance of striation may thus be produced. The cells are united by a small amount of intercellular cementing substance which becomes stained by nitrate of silver. In some parts intercellular spaces may occur, bridged across as in epithelia by fine denticulations of the cells.

They are generally collected into larger and smaller fasciculi, which in many cases cross one another and interlace. The fasciculi are attached at their ends by connective tissue to the membranous and firmer parts where they occur. In some cases the attachment of the plain muscular cells takes place by means of elastic fibres which bifurcate at the end of the muscular cell. The two branches extend along either side of this and are firmly attached to it. In other cases again, according to Watney, the attachment may take place through the medium of connective tissue corpuscles, the branches of which embrace the muscular cell in like manner.

Distribution.—The plain muscular tissue is for the most part disposed in the coats of the membranous viscera. It is met with in the lower half of the gullet, the

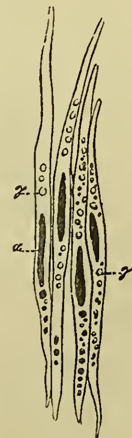


Fig. 348.—Muscular fibre-cells from the uterus three weeks after delivery, treated with acetic acid, magnified 350 diameters. (Kölliker.)
a, nuclei ; γ, fat-granules.

stomach, and the whole intestinal canal ; that is, both in the muscular coat of the alimentary canal, and also as a layer in the tissue of the mucous membrane, and in the villi ; in the trachea and bronchial tubes, in the bladder and ureters, and the ducts of the larger glands generally, in the uterus and its appendages, in the corpora cavernosa of both sexes, in the prostate gland, in the spleen, in the muscle of Müller at the back of the orbit, and in the ciliary muscle and iris. The middle coat of the arteries, the coats of many veins and those of the larger lymphatics contain plain muscular tissue. In the skin it is present in the tubules of the sweat glands, in the form of minute muscles attached to the hair-follicles, and in the dartos or subcutaneous tissue of the scrotum. Numerous nerves, chiefly of the pale variety, are supplied to this tissue ; before their ultimate distribution they frequently come into connection with microscopic ganglia. The tissue receives blood-vessels, but these are far fewer in proportion than those of voluntary muscle. In some situations, as in the wall of the stomach and intestine, abundant lymphatic plexuses are found in close relation to the muscular layers.

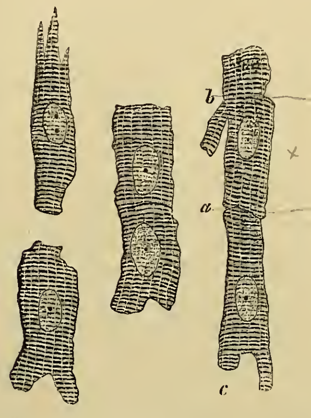
Development.—The elements of the plain or unstriped muscular tissue are derived from embryonic nucleated cells, consisting of the usual granular-looking protoplasm. These cells become lengthened out, pointed at the ends, and flattened with elongation of the nucleus, whilst their substance becomes longitudinally fibrillated and anisotropous, and acquires its permanent condition and characteristic properties.

The great increase in the muscular tissue of the uterus during gestation takes place both by elongation and thickening of the pre-existing fibre-cells of which that non-striated tissue consists, and it is said also by the development of new muscular fibre-cells from small nucleated, granular cells lying in the tissue. In the shrinking of the uterus after parturition the fibre-cells diminish to their previous size ; many of them become filled with fat granules (fig. 348), and eventually many are doubtless removed by absorption.

Regeneration of plain muscle after artificially-produced lesions has been seen to be accompanied by karyokinetic multiplication of the muscle-cells adjacent to the lesion (in the newt by Stilling and Pfitzner).

CARDIAC MUSCULAR TISSUE.

The fibres of the heart (figs. 349, 350) differ remarkably from those of involuntary muscular organs in general, inasmuch as they present transverse striæ. The striæ, however, are less strongly marked, and less regular, and the fibres are smaller in diameter than in the voluntary muscles. They differ also from these in being made up of distinct quadrangular cells (fig. 349) joined end to end and often presenting a branched or forked appearance near one extremity (c). Each cell has a



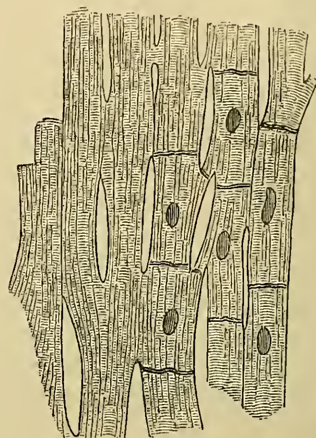


Fig. 349.—Six muscular fibre-cells from the heart, magnified 425 diameters. (E. A. S.)

a, line of junction between two cells ; b, c, branching of cells. From a drawing by Mr. J. E. Neale.

Fig. 350.—Muscular fibres from the heart, magnified, showing their cross striæ, divisions, and junctions. (Schweigger-Seidel.)

The nuclei and cell-junctions are only represented on the right-hand side of the figure.

single clear oval nucleus situate near the centre ; occasionally two nuclei are seen. The cell substance is striated longitudinally as well as transversely, its substance appearing to be composed of a number of parallel columns (sarcostyles), which on transverse section are seen as small polygonal areas. An investing membrane or

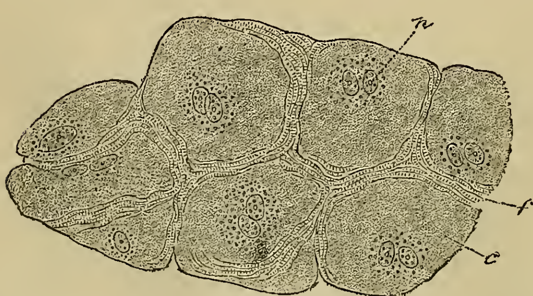


Fig. 351.—Fragment of the network of Purkinje from the ventricular endocardium of the sheep. (Ranvier.) $\frac{300}{1}$.

c, cell ; f, striated substance ; n, nuclei.

sarcolemma has not hitherto been proved to exist on these fibres.

The muscular fibres of the heart freely divide and anastomose (fig. 350), the junctions with neighbouring fibres being effected by the medium of the cell-offsets above noticed.

In the frog and lower vertebrata generally the muscular fibres of the heart are formed of elongated spindle-shaped cells, resembling in shape the cells of plain muscular tissue, but exhibiting distinct transverse striation.

In certain situations, *e.g.*, immediately beneath the lining membrane of the ventricles, the cardiac muscular tissue shows a peculiar modification in the form of a network of clear beaded fibres, just visible to the naked eye, which were described by Purkinje, and are known by his name. When examined with the microscope they are seen to be composed of large clear quadrangular cells; each usually contain two nuclei near the centre, with a little granular protoplasm around the nuclei. At the margin of the cells are columns of transversely striated muscle-substance, which partly surround the cells and appear to join with the muscle-columns of adjacent cells, so as to produce the aspect of an open network of muscular fibres with large cells occupying its meshes. The most probable explanation of this appearance is that these are cells of the muscular tissue the differentiation of which has been arrested at an early stage of their development, and that the cells themselves have continued to grow without any further formation of the cross-striated substance.

Like the skeletal muscles the heart-muscle is richly supplied with blood-vessels. The muscular tissue differs, however, from that of ordinary skeletal muscles in the large supply of lymphatic vessels with which it is provided. The lymphatics, in fact, occupy almost all the interstices of the muscular network, so that the muscular substance is like a sponge, the meshes of which are occupied by lymph. The nerves which are supplied to the cardiac fibres are all non-medullated near their terminations. Their manner of ending will be afterwards considered.

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[1] The student is referred to these articles for the older Bibliography of the subject.

[2] Haycraft has endeavoured to show that the cross-markings upon a muscle-fibre are nothing but the optical effect of varicosities of the component fibrils, since impressions of muscle in collodion reproduce most of the cross-striated appearances. But this fact is entirely insufficient to prove the point, for it is clear that a difference in consistence of the different parts of the muscle-element would alone lead to the reproduction by the impression-method, and in view of the entirely different optical and chemical properties of the different parts of the muscle-element, such a position is quite untenable.

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NERVOUS SYSTEM.

The nervous system consists of a *central part*, or rather a series of connected *central organs*, named the *cerebro-spinal axis*, or *cerebro-spinal centre;* and of the *nerves,* which have the form of cords connected by one extremity with the cerebro-spinal centre, and extending from thence through the body to the muscles, sensible parts, and other organs placed in functional relation with them. The nerves form the medium of communication between these distant parts and the centre. One class of nervous fibres, termed *afferent* or *centripetal*, conducts impressions towards the centre,—another, the *efferent* or *centrifugal*, carries stimuli from the centre to the periphery.

Besides the cerebro-spinal centre and the nervous cords, the nervous system comprehends also certain bodies named *ganglia,* which are connected with the nerves in various situations. These bodies, though of much smaller size and less complex nature than the cerebro-spinal centre, agree, in some respects, with that organ in their elementary structure, and to a certain extent also in their relation to the nervous fibres with which they are connected; and this correspondence becomes even more apparent in the nervous system of the lower members of the animal series.

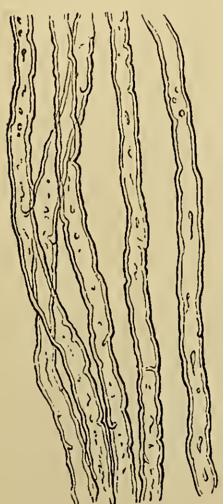
The nerves are divided into the *cerebro-spinal*, and the *sympathetic* nerves. The former are distributed principally to the skin, the organs of the senses, and other parts endowed with manifest sensibility, and the muscles. They are, for the most part, attached in pairs to the cerebro-spinal axis, and like the parts which they supply are, with few exceptions, remarkably symmetrical on the two sides of the body. The sympathetic nerves, on the other hand, are destined chiefly for the viscera and blood-vessels, of which the movements are involuntary, and the natural sensibility is obtuse. They differ also from the cerebro-spinal nerves in having generally a greyish or reddish colour, in their less symmetrical arrangement, and especially in the circumstance that the ganglia connected with them are much more numerous and more widely distributed. Branches of communication pass from many of the spinal nerves at a short distance from their roots, to join, and in fact to form, the sympathetic, which is thus seen to be merely an offset from the cerebro-spinal centre, as indeed its mode of development (see EMBRYOLOGY) would also appear to show.

The nervous system is made up of a substance proper and peculiar to it, with inclosing membranes, nutrient blood-vessels and supporting connective tissue. The *nervous substance* has been long distinguished into two kinds, obviously differing from each other in colour, and therefore named the *white*, and the *grey* or *cineritious*.

When subjected to the microscope, the nervous substance is seen to consist of two different structural elements, viz., *fibres* and *cells*. The fibres are found universally in the nervous cords, and they also constitute the greater part of the nervous centres: the cells on the other hand are confined in a great measure to the cerebro-spinal centre and the ganglia, and do not exist generally in the nerves properly so called, although they are found at the terminations of some of the nerves of special sense, and also interposed here and there among the fibres of particular nerves; they are contained in the grey portion of the brain and spinal cord, and in the ganglia.

NERVE-FIBRES.

Two kinds of nerve-fibres are met with in the body, differing from one another both in their microscopical character and in their more obvious aspect : those of the one kind have received the name of *white* fibres, on account of the appearance which they present when collected in considerable numbers, as in the nerve trunks or white matter of the nerve centres, the others being denominated *grey* fibres. When examined with the microscope it is found that this difference of aspect depends upon the presence or absence of a peculiar sheath to the fibre, formed of a kind of fatty substance, this fatty or medullary substance, as it is termed, giving a dark double contour to the white fibres (when seen by transmitted light), which is



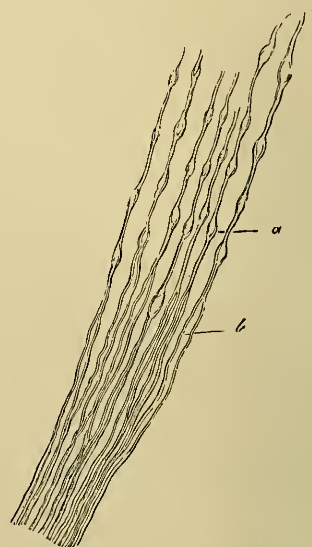


Fig. 352.—White or medullated nerve-fibres, showing the sinuous outline and double contours (after Bidder and Volkmann).

Fig. 353.—A small part of a medullated fibre highly magnified (E. A. S.).

The fibre looks in optical section like a tube—hence the term tubular, formerly applied to these fibres. Two partial breaches of continuity are seen in the medullary sheath, which at these places exhibits a tendency to split into laminæ. The primitive sheath is here and there apparent outside the medullary sheath, and the delicate striæ which are visible in the middle of the fibre probably indicate the fibrillated axis-cylinder.

Fig. 354.—Varicose medullated fibres from the root of a spinal nerve (from Valentin).

altogether absent from those of the other kind. On account of this the white fibres are also known as the *double-bordered* or *medullated* fibres, the grey fibres being termed in contradistinction the *pale* or *non-medullated* fibres, or from their discoverer, the *fibres of Remak*.

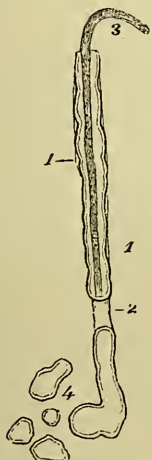
The **medullated nerve-fibres** form the white part of the brain and spinal cord, and by far the greater part of the cerebro-spinal nerves. Viewed singly under the microscope with transmitted light they are transparent, and, as before stated, are characterised by their well-defined even outline and, except the smallest, by their double contour, which gives them a tubular aspect.

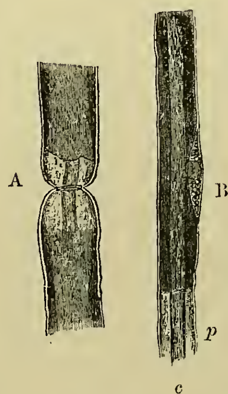
Their size differs considerably even in the same nerve, but much more in different parts of the nervous system ; some being less than $\frac{1}{12000}$th inch ($2\,\mu$), and others upwards of $\frac{1}{1500}$th inch ($17\,\mu$) in diameter. Speaking generally, they

may be divided into three sets or kinds according to their size. Thus, most fibres which are found in the ordinary or cerebro-spinal nerves are from 8μ to 16μ in diameter; whereas those which pass from the roots of the spinal nerves to the sympathetic average only from $1{\cdot}8\mu$ to $3{\cdot}6\mu$, while fibres of an intermediate size occur in large numbers in the vagus, the glosso-pharyngeal, the facial, and in the motor root of the fifth nerve as well as in the anterior roots of the spinal nerves (Gaskell). These differences are illustrated in fig. 384, p. 329.

Many of the medullated nerve-fibres appear dilated or swollen out at short distances along their length, and contracted in the intervals between the dilated parts. These fibres, however, are naturally cylindrical like the rest, and continue so while they remain undisturbed in their place; and the varicose character is occasioned by pressure or traction during the manipulation, which causes the soft matter to accumulate at certain points, whilst it is drawn out and attenuated at others (fig. 354), The fibres in which this is most apt to occur are usually of small size, ranging from $\frac{1}{12000}$ to $\frac{1}{3600}$th of an inch in diameter; and when a very small fibre is thus affected, the varicosities appear like a string of globules held together by a fine transparent thread.

Structure of medullated fibres.—The medullated fibres are composed for the most part of three distinct structures, viz., an axial fibre (the *axis-cylinder* of





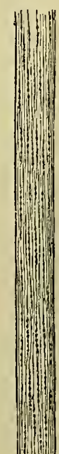


Fig. 355.—Diagram to show the parts of a medullated fibre, viz., 1, 1, outer or *primitive sheath* enclosing the doubly contoured *white substance* or *medullary sheath*. 2, a part where the white substance is interrupted, the outer sheath remaining. 3, *axis cylinder* projecting beyond the broken end of the tube. 4, part of the contents of the tube escaped.

Fig. 356.—Two portions of medullated nerve fibres, after treatment with osmic acid, showing the axis-cylinder, and the medullary and primitive sheaths (Key and Retzius).

A. Node of Ranvier. B. Middle of an internode with nucleus.

c, axis-cylinder, projecting at the broken end; *p*, primitive sheath within which the medullary sheath, which is stained dark by the osmic acid, is somewhat retracted.

Fig. 357.—Part of an axis-cylinder, highly magnified, showing the fine varicose fibrils within it (Max Schultze).

Purkinje), enclosed within two sheaths, one of these being the *medullary sheath* already mentioned, and the other a delicate membranous tube outside of all, termed the nucleated *sheath of Schwann*, the *primitive sheath*, or the *neurolemma*.[1] But there are medullated fibres in which the primitive sheath is absent, and other fibres and prolongations of fibres in which there is no sheath whatever to the axis-cylinder.

[1] The term neurilemma or neurolemma was formerly applied to the connective tissue sheath of the funiculus (see p. 325), which is now known as the perineurium.

But the latter is always present, and is indeed the chief functional constituent of the nerve-fibre. The several parts of which the nerve-fibre is composed may now be described in detail.

Axis-cylinder.—The essential part of every nerve-fibre is a pale and somewhat indistinct strand, which runs in the axis of the fibre and is termed the *axis-band*, *axial fibre*, or more commonly the *axis-cylinder* (fig. 355, 3 ; and 356, *c*). This essential part is usually enclosed, as just mentioned, in one or more sheaths, but these are not always present, especially at the origin and termination of a nerve-fibre ; and even in the course of the fibre they may be interrupted at intervals. The axis-cylinder, on the other hand, undergoes no interruption along the whole course of the nerve, from the nerve-centre to the peripheral distribution. It appears further to be clearly established that the axial fibre of a nerve is in every case a direct prolongation of a branch of a nerve-cell. It is therefore to be looked upon in the light of a far-extending cell-process ; and the study of the development of the nerve-fibre affords a direct confirmation of this view of its nature.

In the fresh state, and under high powers of the microscope, the axis-cylinder presents an appearance of longitudinal striation, indicating a fibrillar structure (fig. 357) ; and at the termination of the nerves it may often be seen to separate into a number of exquisitely fine filaments or fibrils. These, the *primitive fibrillæ* of Max Schultze, are embedded in a homogeneous or finely-granular material, and may with some reason be regarded as constituting the essential or conducting part of the axis-cylinder, and therefore of the nerve ; at least, it frequently happens that they form the only visible portion of the nerve-fibre that is prolonged to the ultimate termination. The fibrils often exhibit minute varicosities which are highly characteristic in appearance. They have a remarkable affinity for gold salts, and when placed first in solutions of these and afterwards in reducing agents (or merely exposed to the light in water), the metal becomes deposited in the nerve-fibrils, giving them a dark violet, almost black, appearance (see fig. 407, p. 346). They also become deeply stained by methyl blue, especially when it is injected into the vascular system of the living animal (Ehrlich). These methods are employed to trace the mode of ending of the fibrils.

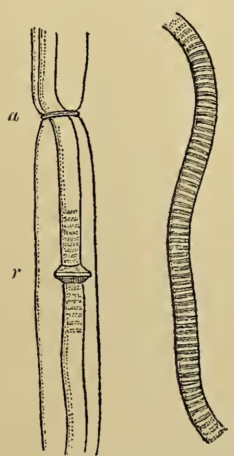


Fig. 358.—Nerve-fibres stained with nitrate of silver to show Frommann's markings in the axis-cylinder. (Ranvier.)

A, fibre showing a node, *a*, with the constricting ring. The axis-cylinder has become shifted, and the part which was opposite the node and which is stained by the silver, is now below it ; *r*, conical enlargement of the axis-cylinder.

B, Isolated axis-cylinder.

The axis-cylinder is, by some authors, stated to be invested with a very delicate structureless sheath. This sheath, which was first described by Mauthner, may possibly be a protoplasmic inner layer of the medullary sheath ; but it is somewhat doubtful whether the appearance is not due to a layer of fluid which has become expressed by a shrinking of the axis-cylinder and coagulated under the influence of the reagents employed.

It was shown by Frommann that after treatment with nitrate of silver and subsequent exposure to the light the axis-cylinder becomes stained in such a manner as to exhibit a distinct cross-striated aspect (fig. 358), but it is not known whether this depends upon any structural feature of the fibre or not. In addition to this cross-striated appearance, which may be seen in any part of the axis-cylinders, they exhibit a peculiar biconical enlargement at each node

of Ranvier when thus treated, the enlargement corresponding in situation to the annular constricting band of the node (Ranvier).

It is not always easy to distinguish the axis-cylinder in the medullated fibres when they are examined in the fresh condition, but it can generally be made manifest by staining the nerve with carmine or hæmatoxylin. In a transverse section of a nerve thus stained the axis-cylinders appear in the form of round or oval areas occupying the centre of the fibres (fig. 362), but they are often much shrunken. The fibrils of the axis-cylinder have a tubular aspect in a well prepared section, which is distinctly visible in photographs under a high power.

Fig. 359.—Portions of two nerve-fibres stained with osmic acid (from a young rabbit). 425 diameters (E. A. S.).

R, R. Nodes of Ranvier, with axis-cylinder passing through. *a*, Primitive sheath of the nerve ; *c*, opposite the middle of the segment indicates the nucleus and protoplasm lying between the primitive sheath and the medullary sheath. In A the nodes are wider, and the intersegmental substance more apparent than in B. (From a drawing by Mr. J. E. Neale.)

Medullary Sheath.—The myelin or substance of the medullary sheath (which was termed the white substance by Schwann on account of its presence being the chief cause of the whiteness of the nerves), undergoes peculiar changes on exposure of the nerve to the action of water and other fluids, so that the outline of the fibre is often rendered uneven ; round and irregular spots appear at various points, the medullary sheath acquiring eventually a confusedly curdled aspect.

The thickness of this sheath varies within wide limits, and indeed this is the chief cause of the variation in size of the medullated nerve-fibres, although the axis-cylinder may also vary in diameter to a considerable extent. In some fibres, the medullary substance forms an exceedingly thin layer, so as to be scarcely distinguishable except by the darker outline which it imparts to the fibre, or it may only occur in parts, these alternating irregularly with other parts in which there is a complete absence of white substance. Such fibres, which are common in some parts of the sympathetic system (fig. 365, *m*, *m*), may be regarded as transitional between the white and the grey fibres.

Nodes and internodes of Ranvier.—It was shown by Ranvier, that there constantly occur in the peripheral medullated nerve-fibres, breaks in the continuity of the white substance, which succeed one another at regular intervals along the course of the nerves, and give the fibres the appearance of being constricted at these places. These *constrictions* or *nodes of Ranvier*, as they may conveniently be termed, divide the fibre into a series of *internodes* of nearly equal length. The segmentation is readily made apparent by the action of a solution of osmic acid, which leaves the nodes (fig. 359, R, R ; fig. 360) almost colourless, while the medullary sheath, or white substance of Schwann, becomes stained of an inky black colour.

The white substance of the medullary sheath is often found to have shrunk somewhat in the neighbourhood of a node (fig. 356, A), and it can then be seen that there is present, in addition to it, a clear or finely granular stroma, which has become evident in consequence of retraction of the fatty substance which normally pervaded it.

The outer or membranous sheath of the fibre (neurolemma) appears to be continued over the nodes, for when a medullated fibre is examined in water and the substance

of the medullary sheath exudes from the cut ends of the nerve-fibres, it is found that the place of that which thus escapes is taken by the white substance from the next internode ; and this substance may be seen to flow past the constrictions of Ranvier without escaping at those points. Within the primitive sheath the internodes are united by an annular disc—the "constricting band" of Ranvier—the nature of which is unknown, although like intercellular substance elsewhere, it becomes stained by nitrate of silver. The last-named reagent stains also the axis-cylinder in the neighbourhood of the node in the manner indicated by Frommann (see page 310), so that the fibres after this treatment appear marked with little crosses (fig. 381) ; the transverse limb of the cross being due to the ring of inter-segmental substance, the longitudinal to the axis-cylinder. Many other fluids stain the axis-cylinder at the nodes only, being prevented from reaching it elsewhere owing to the presence of the fatty matter in the surrounding medullary sheath.

The division of nerve-fibres always occurs at the site of a node of Ranvier (see fig. 388, p. 333).

Engelmann argues in favour of a discontinuity of the axis-cylinder (as well as of the medullary sheath) at the nodes of Ranvier, basing his argument partly on the fact that the

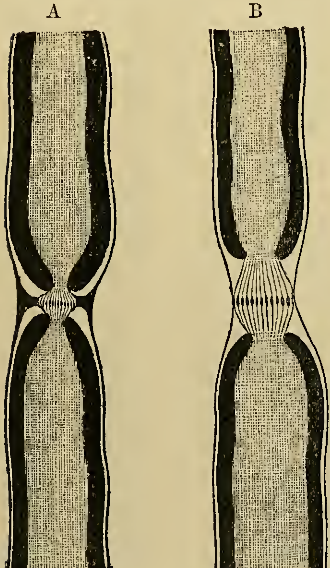


Fig. 360.—Nodes of Ranvier from the nerve of a pigeon, treated with osmic acid. (v. Gedoelst.)

The medullary sheath is stained black. The fibrils of the axis-cylinder have enlargements at the middle of the node. In A the constricting band is seen.

degeneration which results above the section when a nerve-fibre is cut, stops at the first node of Ranvier, partly on appearances obtained after a certain method of treatment with nitrate of silver, a dark deposit characteristic of inter-cellular substance traversing, according to the account given by him, the thickness of the axis-cylinder at the nodes. He also points out that the axis-cylinders very readily become broken across at the nodes. This view has been in a measure confirmed by the researches of Gedoelst, who has shown that there is a tendency at the nodes of Ranvier for the fibrils of the axis-cylinder to develop minute swellings or nodosities which closely resemble those which are formed upon the achromatic fibres which unite the two daughter-nuclei of a dividing cell in most vegetable and some animal tissues (*Zell-platte* of Strasburger) and which indicate the plane of separation between the two daughter-cells and of formation of the cellulose or other membrane. Such a structure is shown in the representations of a dividing ovum given by Strasburger (see fig. 218, p. 188), and is superficially very similar to that figured by Gedoelst upon the axis-cylinder at the nodes (fig. 360). But the identity of the two structures in spite of this superficial resemblance must not be taken as proved. The axis-cylinder is not an out-growth from a nucleus, nor can its segments be taken to represent nuclei. Neither do its fibrils resemble in chemical characters so far as is known the achromatic fibrils of a cell-nucleus. But in spite of these differences the correspondence between an inter-node of a nerve and an elongated cell is so direct and obvious that a view which permits of the presence of the nodes of Ranvier being explained as indicating a tendency of the fibre to become divided across into cell-segments cannot be altogether disregarded. Ranvier, Boveri, and others, have looked upon the medullary and primitive sheaths only as being thus segmented up into cells, which they regard as wrapped around the axis-cylinder. But when first developed the medullary sheath is a continuous and unsegmented layer, and appears to be laid down upon the surface of the pale fibre which is becoming medullated, by the superficial protoplasm of that fibre itself (see Development of nerves).

The internodes or nerve-segments vary in length in different nerves ; in larger nerve-fibres they may perhaps, speaking roughly, average about 1 mm. In the nerves of young animals they are often much shorter than this, so that the growth

of nerves in length with the growth of the limbs and other parts of the body is in part due to interstitial elongation of the segments.

In the middle of each internode an oval nucleus lies embedded in the medullary

Fig. 361.—MEDULLATED NERVE-FIBRE TREATED WITH OSMIC ACID (Key and Retzius).

A node of Ranvier (E) and a nucleus (K) is represented. The medullary sheath appears broken up into a number of segments with conical or funnel-shaped ends fitting into one another.

sheath (figs. 356, B, 359, *c*, 361, K); these nuclei will be described with the primitive sheath.

Medullary segments.—Other breaks of continuity are seen in the medullary sheath (figs. 353, 361) which are of an entirely different nature from the nodes of Ranvier; indeed it is somewhat uncertain how far they correspond to a pre-existent structure in the fibre. In consequence of their presence the medullary sheath appears as if made up of a number of small cylindrical segments with either conical or funnel-shaped ends which fit in with one another in the alternate segments. The segments in question have been frequently described as integral constituents of the medullary sheath (Schmidt, Lantermann and others). It is easy to convince oneself of the reality of the appearances here mentioned, but it is far less easy to be certain that they are not artificial productions. Against the view of their existence in the natural condition it is to be noted that they are extremely variable in number and in size in a given length, even of the same nerve-fibre, that they appear to become increased in number if the nerve-fibre have been subjected to much manipulation, that they have no constant relation, so far as can be made out, to the other parts of the medullated fibre, and that, according to the testimony of several careful observers, they are not to be seen in the nerve-fibres of the living animal, unless these have been subjected to an abnormal amount of traction or other mechanical injury. This last assertion is denied, however, by others, who maintain the pre-existence of the medullary segments, and describe them and the oblique clefts which separate them as definite parts of the sheath. Ranvier on the other hand, who first described the original protoplasmic condition of the medullary sheath, considers that the protoplasm has disappeared and become replaced by the pseudo-fatty substances (lecithin, neurin, &c.), except next to the primitive sheath or neurolemma, and next to the axis-cylinder, where fine layers still remain, and he regards these as being connected with one another by protoplasmic septa, which lie in the intervals between the conico-cylindrical segments of the medullary sheath. In short he regards each segment of the medullary sheath as representing an elongated cell occupied mainly by this fatty material and wrapped round the axis-cylinder.

Careful examination of the fibres in the fresh condition reveals fine obliquely disposed lamellæ, which in optical section have the appearance of fibres, bridging across the clefts between the segments (fig. 353). In nerve-fibres which have been treated by a mixture of bichromate of potash and osmic acid, and afterwards by nitrate of silver, the situation of each cleft is occupied by what looks like a thread of darkly stained substance passing spirally around the fibre (Rezzonico, Golgi). The meaning of these appearances is by no means clear.

Rod-like and reticular structures in the medullary sheath.—It was

shown by McCarthy that after a nerve has been hardened with chromate of ammonium (picric acid is still better adapted for the purpose) the medullary sheath appears pervaded with minute rod-like structures which pass radially between the axis-cylinder and the primitive sheath in such a manner as to give the cross-section

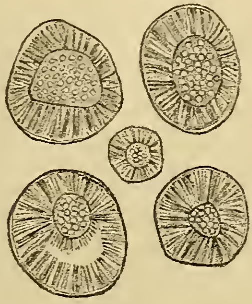


Fig. 362.—Section across part of a nerve-trunk, showing the sections of the nerve-fibres (E. A. S.). $\frac{1000}{1}$ (From a photograph.)

The nerve was hardened in picric acid and stained with picrocarmine. The radial striation of the medullary sheath is very apparent. In one fibre the axis-cylinder is shrunken and the medullary striations are broken. The fibrils of the axis-cylinder are clear in section and suggest a tubular structure.

of a nerve-fibre the appearance of a wheel. The rods stain with carmine and hæmatoxylin, which do not colour the fatty substance of the medullary sheath. In nerves stained with osmic acid (in which these structures were first detected by Lantermann) they are far less easily seen, in consequence of the dark colouration of the fatty substance in which they are embedded. The apparent rods are not distinct from one another, but are united, for it is not possible to isolate them as separate elements.

If a nerve is first placedin strong alcohol and then subjected to the action of staining fluids, it will be found that the rod-like structures are not visible as such, but

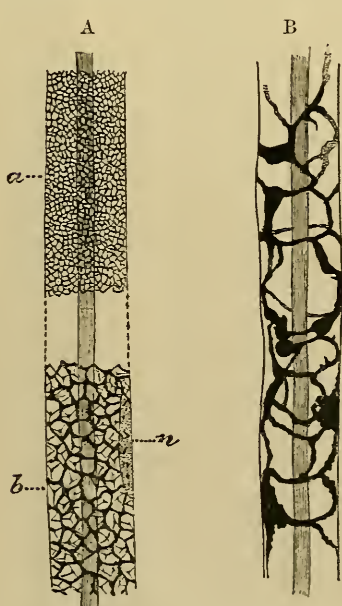


Fig. 363.—Nerve-fibres showing reticular appearances in the medullary sheath (Gedoelst).

A. A nerve-fibre from the toad, showing different appearances of the network at different parts of its course.
B. A nerve-fibre from the guinea-pig, showing a much coarser network. *n*, nucleus of fibre.

the medullary sheath appears pervaded instead by a finely reticular structure, which like the rods, becomes readily stained by most dyes. The network thus obtained is considered by Kühne and Ewald, who first drew attention to it, to be chemically of a horny nature, on account of the resistance it offers to reagents, and especially to digestive ferments, and they have accordingly designated it the horny reticulum or neurokeratin network. They further describe it as continuous with two delicate membranes of a similar nature, one immediately investing the axis-cylinder and the other lining the primitive sheath. The pre-existence of a neurokeratin network is, however, at least questionable. Of the presence both in the nerves and in the white matter of the nerve-centres of the material known as neurokeratin there can be no doubt; it appears probable, however, that its reticular arrangement is a product of the reagent (alcohol) employed to demonstrate it. This at least has been the opinion of most authors who have investigated the subject (Hesse, Pertik, Waldstein and Weber), whereas others, whilst admitting its variability, consider its pre-existence beyond doubt. Gedoelst, who maintains this view of the neurokeratin network, regards it as the reticulum of the original protoplasmic cell from which the medullary sheath of the nerve-segment has been formed. It must be admitted, however, that its

extreme variability of appearance and size of mesh (fig. 363) even in the course of the same nerve-fibre, lends much probability to the view that it is produced artificially by the precipitation by the reagent employed, of some material entering into the constitution of the myelin of the medullary sheath. Gerlach has in fact shown that the character of the reticulum varies with the strength of the alcohol employed to act upon the nerve.

It will be seen from the above that there is still much diversity of opinion with regard to the minute structure of the medullary sheath of the nerves. As to its chemical composition, the white substance or myelin consists chiefly of lecithin and neurin together with cholesterin and one or two other substances in less amount. When escaped from the nerve-fibres it forms drops either rounded or irregular in shape, which always show the double contour which is so characteristic of the medullated nerve-fibres, the appearance being due to the peculiar manner in which myelin refracts the light. In contact with water it combines with that fluid, and as a result of the imbibition the myelin-drops undergo a considerable increase in bulk, accompanied by remarkable changes of form, often growing out into tube-like filaments for a considerable distance into the fluid. In this behaviour myelin is not peculiar but resembles certain other substance of a fatty and resinous nature.

It is generally believed that medullated nerve-fibres occur only in vertebrates, but Retzius has described the nerve-fibres in Palæmon (a crustacean) as also possessing a myelin-sheath, with nodes and internodal nuclei.

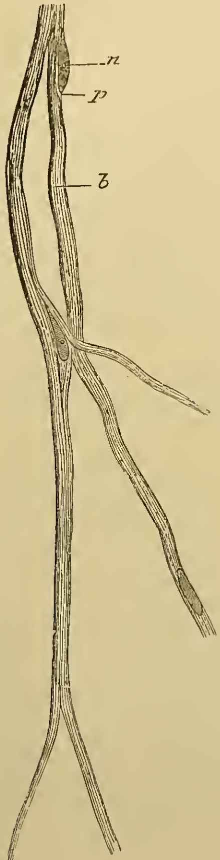
Sheath of Schwann, primitive sheath, or neurolemma.—The sheath of Schwann forms the outermost covering of the white nerve-fibres. It has the appearance of a delicate homogeneous membrane with nuclei disposed at intervals along its inner surface. As already mentioned, these nuclei bear a definite relation to the segments of the nerve-fibre, for they lie about midway between the nodes, only one nucleus being found in each internode (fig. 359). The nuclei are oval and sometimes flattened, they usually lie in a depression of the medullary sheath, and at each end of the nucleus, especially in young nerves, there is a small amount of granular protoplasm which may spread for a short distance between the primitive and the medullary sheath. The primitive sheath usually dips in at the nodes and is there only separated from the axis-cylinder by the annular band of Ranvier before mentioned.

So long as the primitive sheath is accurately filled by the contained medullary substance its outline can seldom be distinguished, but sometimes, when the white substance separates at various points from the inside of the tube, the contour of the fibre becomes indented and irregular, and then the membrane in question may, in favourable circumstances, be discerned as an extremely faint line, running outside the deeply shaded border formed by the white substance.

In the white fibres of the brain and spinal cord the nucleated sheath is absent, and these are only invested by a medullary sheath. In consequence of the absence of the comparatively tough primitive sheath the fibres from these situations cannot be isolated for any distance without rupture, and it is found that for the same reason the medullary sheath readily breaks away from the axis-cylinder, so that this is thus left bare. It is usually stated that the nodes of Ranvier do not exist on these white fibres of the brain and spinal cord; but various observers have described appearances which seem to indicate that the nodes may be present in these fibres also.

Pale or non-medullated fibres; fibres of Remak.—These occur principally in branches of the sympathetic nerve, but they are found also in greater or less amount in the cerebro-spinal nerves. They are transparent, faintly striated fibres of varying size, which exhibit nuclei at frequent intervals. The nuclei are applied to the surface of the fibre, and, according to the generally received account, belong to a delicate homogeneous sheath, similar to the primitive sheath of the medullated fibre. It must be admitted, however, with Ranvier that it is difficult or impossible to exhibit the sheath, and if this is the case, the nuclei must be regarded as embedded in the peripheral layer of the fibre itself, and as belonging to this. Many of these

fibres are branched and united with neighbouring fibres, so as to form a network along their course ; a condition which is never found in the course of the medullated



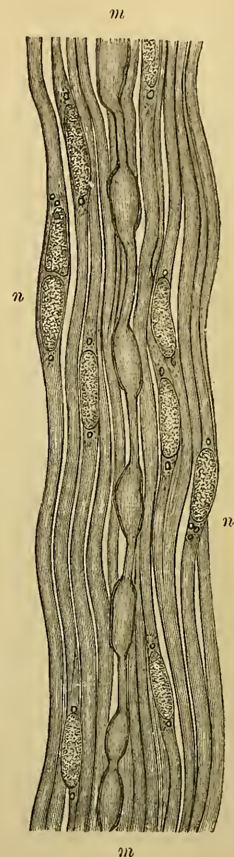


Fig. 364.—Portion of the network of fibres of Remak from the pneumogastric of the dog (Ranvier).

n, nucleus ; *p*, protoplasm surrounding it ; *b*, striation caused by fibrils.

Fig. 365.—A small bundle of nerve fibres from the sympathetic nerve (Key and Retzius).

The bundle is composed of pale nerve-fibres, with the exception of the fibre *m*, *m*, which is enclosed here and there by a thin medullary sheath ; *n*, *n*, nuclei of pale fibres.

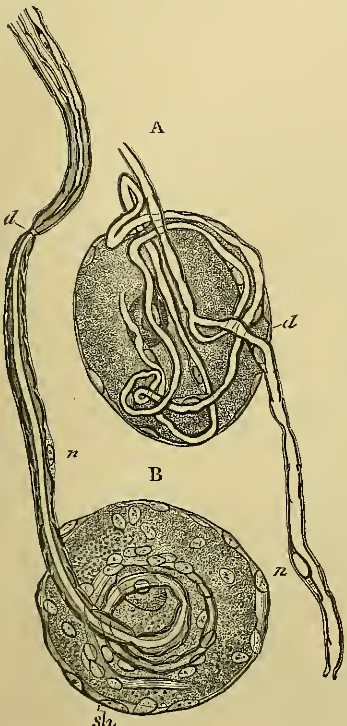
nerves. The branches of the olfactory nerve consist wholly of pale fibres, but these are different from the ordinary pale fibres in being provided with a distinct nucleated sheath.

NERVE-CELLS.

These are found in the grey matter of the brain and spinal cord and in the ganglia ; they exist also in some of the nerves of special sense near their terminations, and occur here and there in the course of certain other nerves. They are often named ganglion-cells.

In shape, nerve-cells vary greatly. Thus they may be spheroidal or ovoidal with a general even outline, or they may be of an angular or irregular figure, and it is found that the nerve-cells have a characteristic shape in certain parts of the

nervous system. For example, the cells from the spinal ganglia of man and most vertebrates are of a rounded shape (see fig. 366), those from the sympathetic ganglia are more angular (fig. 367), those from the grey matter of the spinal cord of an irregular form, and provided with numerous branching processes (fig. 368); those from the cerebral convolutions conical, those from a particular layer of the



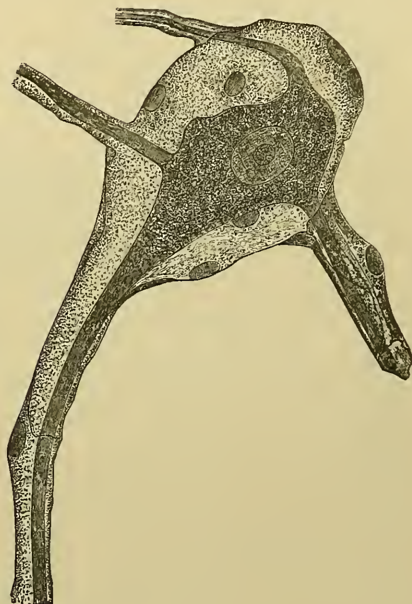


Fig. 366.—Two nerve-cells from a spinal ganglion (human) (Retzius).

sh, nucleated sheath; *n*, *n*, nuclei of the primitive sheath of the nerve. From each cell a fibre can be seen to arise, and after a convoluted course on the surface of the nerve-cell, to bifurcate (opposite *d*); from which point the divisions pass either in the opposite direction to one another, as in A, or at first in the same direction as in B. The nuclei of the sheath of the nerve-cell are all represented in B, but only those seen in profile have been represented in A.

Fig. 367.—A ganglion-cell within its sheath; from the human sympathetic. Highly magnified. (Key and Retzius.)

grey matter of the cerebellum, flask- or retort-shaped (fig. 374, *c*), and so on. Other cells, situated in the course of certain nerve-fibres, are somewhat spindle-shaped, the two poles of the spindle being prolonged into the nerve-fibre.

Nerve-cells vary much in size as well as in shape. Many of the nerve-cells in the body are very large, but there are others which are quite small. The latter are especially abundant in the deeper part of the grey matter of the cerebellum and in the retina, where they form what are known as the granule-layers (fig. 374, *d*).

Structure.—The nucleus of a nerve-cell is usually a large clear round vesicle containing a very distinct highly refracting nucleolus, and, in some cases, an intra-nuclear net-work. The cell-substance is finely granular or punctated, sometimes indistinctly striated, or reticular in appearance. Cells are often to be seen which contain very distinct brown or yellow coloured patches caused by an accumulation

of pigment granules (fig. 372, *b*). The colour is deeper in adult age than in infancy.

Every nerve-cell has one or more processes, and the cells are often named according to the number of processes they possess, uni-, bi-, and multi-polar ; terms not perhaps well chosen, but rendered current by use. A fibrillation similar to that in the axis-cylinder of a nerve-fibre is visible in the cell-processes, and it may also be traced passing from them into the body of the cell and even through this from

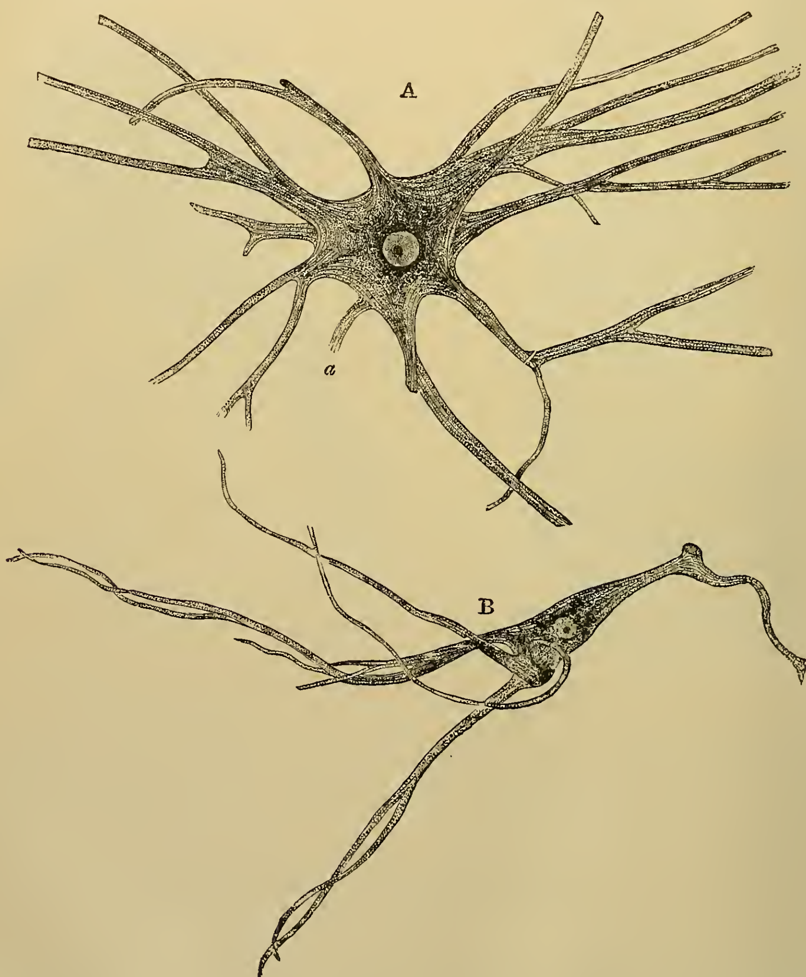


Fig. 368.—Two nerve-cells from the spinal cord of the ox, isolated after maceration in very dilute chromic acid. Magnified 175 diameters. (E. A. S.)

Each cell has a well-defined, clear, round nucleus, and a large nucleolus. The cell-processes are seen to be finely fibrillated, the fibrils passing from one process into another through the body of the cell. *a*, axis-cylinder process broken a short distance from the cell.

one process into another (fig. 368). Some affirm that they have been able to trace a connection of these fibrils with the nucleus of the cell, but this is at present doubtful.

Nerve-cells which are entirely destitute of processes have sometimes been described. It is possible that such may exist, but there is always a probability that these may

be cells, the processes of which have become broken away during the manipulation required for isolation.

Fig. 369.—A nerve-cell from the cerebral cortex (Golgi).
a, axis-cylinder process.

Fig. 370.—A bipolar nerve-cell, with its poles prolonged into medullated nerve-fibres (Key and Retzius).
The whole is invested by the primitive sheath. *R*, *R*, nodes of Ranvier.

It has been shown that many cells have at least one of their processes prolonged as a nerve-fibre (axis-cylinder process) and the statement is probably true of all

developed nerve-cells. In the case of the bi-polar cells, especially those of a spindle-shape with a process from either end, both these processes are prolonged as nerve-fibres (fig. 370) : from another point of view the cell might be looked upon as a nucleated enlargement interpolated in the course of the fibre. In other bi-polar

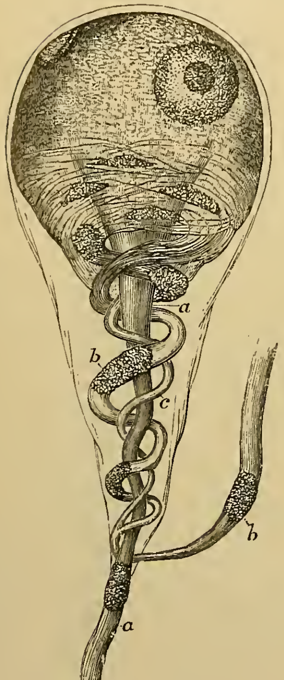


Fig. 371.—Ganglion-cell of a frog, highly magnified (Beale).
a, *a*, straight fibre ; *b*, *b*, coiled fibre ; *c*, smaller coiled fibre joining it.

Fig. 372.—Ramified nerve-cell from anterior cornu of spinal cord of man (from Gerlach).
a, axis-cylinder process. *b*, clump of pigment granules. Above the cell is seen part of the network of fibrils mentioned in the text (p. 322).

Fig. 373.—Axis-cylinder process of a nerve-cell (M. Schultze).
×, ×, Portion of nerve-cell from spinal cord of ox, with axis-cylinder process, *a*, coming off from it and acquiring at *a′* a medullary sheath. Highly magnified.

cells in which the processes come off on the same side of the cell, the latter often has a pyriform shape (fig. 371), the fibres being prolonged from the stalk of the pear and the nucleus of the cell being placed in the larger end. As was shown by Beale, a peculiar arrangement of the two fibres which are thus prolonged from these pear-shaped cells is found, the one being generally coiled spirally round the other for a certain distance, after which the fibres separate and take opposite directions. The spiral fibre has been described as breaking up into an interlacement of fine fibrils upon the surface of the cell. An indication of this is represented in fig. 371.

Cells of this kind are met with occasionally in the sympathetic ganglia both of the frog (where they were first discovered by Beale) and of the mammal.

In multi-polar cells either one or more of the cell-processes may be prolonged into nerve-fibres. In the large ramified nerve-cells of the anterior cornu of the spinal cord only one of the many processes is prolonged into a nerve-fibre. This is known as the axis-cylinder process of Deiters (figs. 372, 373, *a*), and is distinguished from the other processes of the cell by being unbranched and of a somewhat clearer and more evenly fibrillated appearance than the other processes, which branch again and again, becoming finer as they proceed, until they are eventually lost to sight in the grey matter.

The ramified cell-processes have been regarded by Golgi as representing rootlets by means of which the cells penetrate into and derive nutriment from the surrounding grey matter. With this idea he has termed them the "protoplasmic" processes as distinguished from the nerve-fibre process or processes. Although there does not seem to be sufficient evidence in favour of this view; and the intimate relationship which obtains between the ramified processes of different nerve-cells may still be considered to point to these processes as a means of transmission and diffusion of nerve impulses in the grey matter, the view which was formerly entertained that the ramified processes are united with one another into a network pervading the grey matter is not substantiated by the employment of the most recent methods of research, although these methods permit of the following out of the processes of a nerve-cell to a much greater extent than any that had been previously in use. In all cases the processes appear to end after a number of branchings in free terminations: the branchings may be closely interlaced with those of neighbouring cells, but to all appearance remain anatomically distinct from them.

The axis-cylinder process of a nerve-cell is distinguishable from the other processes not only in the fact that as a rule it does not, like those, undergo a dendritic ramification near the cell from which it takes origin, but also, as was shown by Golgi, in giving off, at right angles to its course, minute lateral fibrils at frequent intervals (fig. 369, *a*). These lateral fibrils lose themselves in the surrounding nervous matter; they perhaps come into relation with similar fibrils from other cells or from nerve-fibres, but both their actual mode of termination and their functional significance are at present unknown. According to Flechsig they become medullated.

Ultimately even the axis-cylinder processes of the nerve-cells undergo dendritic ramification. This is seen in the terminal ramification which is the usual mode of ending of both motor and sensory nerve-fibres, and in the ramification of branches from the posterior root-fibres in the grey matter of the spinal cord (see fig. 383, p. 328). Sometimes this ramification of the axis-cylinder process occurs nearer to the body of the cell, as in the case of the cells of the outer layer of grey matter of the cerebellum, in which the axis-cylinder processes, after a longer or shorter course, break up into one or more close dendritic ramifications which envelope the cell-bodies of the corpuscles of Purkinje (fig. 375).

Some multi-polar cells, many of those in the ganglia for instance, possess two, three, or more nerve-fibre processes and no protoplasmic processes (fig. 367). Sometimes these axis-cylinder processes of a nerve-cell, especially those in the sympathetic, are continued along their whole course as pale nerve-fibres. But in most cases, at a short distance from the body of the cell, they acquire a medullary sheath and become in fact medullated nerve-fibres (fig. 373, *a'*). In the bi-polar cells (those at least of a pyriform shape), the one fibre may be prolonged as a pale fibre, the other may be a medullated fibre. In other instances both fibres may be medullated or non-medullated. In multi-polar cells of the sympathetic ganglia one process may be continuous with one of the small medullated fibres which enter these ganglia, and the others with non-medullated fibres which pass from the ganglia to the peripheral distribution of the nerves. In this manner the cells may act as distributing centres multiplying the paths of the nervous impulses towards the

periphery, and furnishing at the same time the points of union between the medullated and non-medullated fibres. In the uni-polar cells of the ganglia upon the posterior roots of the spinal nerves, and in some other situations the single process (which may be much convoluted near the cell and soon acquires a medullary sheath) bifurcates after a longer or shorter course, and its two branches are eventually prolonged in opposite directions along the nerve (fig. 366).

The nerve-cells in the brain and spinal cord resemble the nerve-fibres in the same parts in being destitute of any nucleated sheath, but in the ganglia each nerve-cell is enclosed in a membranous capsule, having nuclei on its inner surface and apparently continuous with the nucleated sheath of the nerve-fibre or fibres with which the cell is connected (fig. 367).

Sustentacular tissue of the nerve-centres; neuroglia.—In the grey matter of the cerebro-spinal centre, the nerve-cells appear at first sight as if imbedded in a sort of matrix of granular substance, interposed between them in greater or less quantity, and traversed in all directions by nerve-fibres. But the appearance of

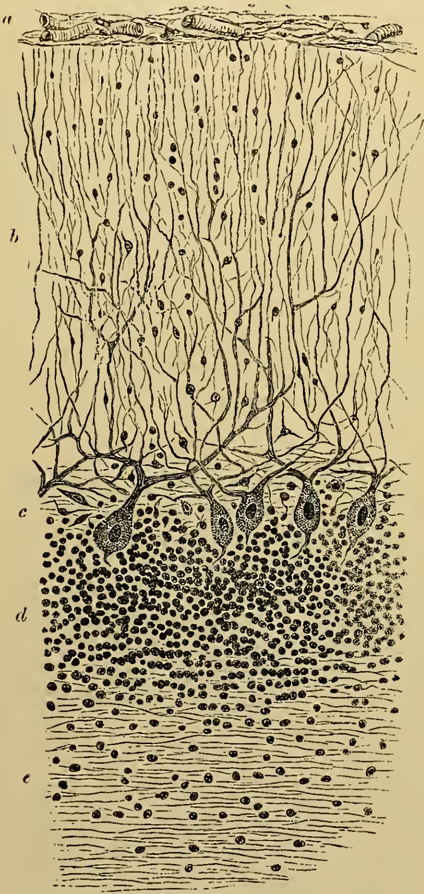


Fig. 374.—Structure of cortex of cerebellum (Sankey).

a, pia mater; *b*, external layer; *c*, layer of corpuscles of Purkinje; *d*, inner or granule layer; *e*, medullary centre.

Fig. 375.—From a section of cerebellum, stained by the method of golgi (Ramón y Cajal).

The figure shows the basket-work of ramifications of the cells of the outer layer of grey matter, enveloping two corpuscles of Purkinje.

a, axis-cylinder process of one of the corpuscles; *b*, basket-work of fibres derived from the axis-cylinder processes, *c*, of cells of the outer layer.

granular or molecular matter results from a confused interlacement of fine fibrils and especially of the fine ramifications of nerve-cells, and of the special sustentacular cells immediately to be described; or from the crushing and breaking down of such fibres in the process of examination.

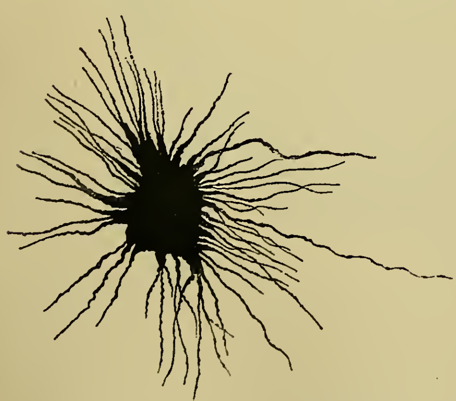
The supporting substance which is met with in the white matter of the brain and spinal cord between the nerve-fibres also looks in section like a network, although rather more open than that in the grey matter. It was supposed by

Kölliker to be a form of retiform tissue; accordingly he named it the *reticulum* of the nervous centres, but the term *neuroglia* which was proposed by Virchow has been more generally adopted. It is not, however, of the nature of connective tissue, for it contains neither the characteristic fibres nor cells of that tissue; nor is it developed from mesoblast but from the neural epiblast. The neuroglia is, in fact, composed entirely of greatly ramified cells (glia-cells), the branches of which pass everywhere in the interstices of the proper nervous elements, and are somewhat modified in their general arrangement according to the nature of the elements which they chiefly support. Thus in the white matter of the spinal cord the branches of the neuroglia-cells can be seen bending round the medullated nerve-fibres and accommodating themselves exactly between them like packing material between parallel glass tubes (fig. 376). In the cerebral cortex, on the other hand, where the arrangement of the nervous elements is much less regular, the branches of the glia-cells have a dense brush-like arrangement such as is shown in fig. 377.

Fig. 376.—A neuroglia-cell from the white substance of the spinal cord stained by Golgi's method (E. A. S.).

It has been shown by Ranvier that the glia-cells are fibrillated, the fibrils passing through the body of the cell from one cell-process to another. These are seen in fig. 378, which represents a glia-cell from the spinal cord isolated after maceration in dilute alcohol.

In addition to these stellate neuroglia-cells a further support is afforded to the nervous matter of some parts of the central nervous system by the ramified prolongations of the ciliated epithelium-cells which line the central canal (spinal cord, &c.). These prolongations extend originally to the outer surface of the spinal cord, and for a considerable period of its early development they can be traced as fine



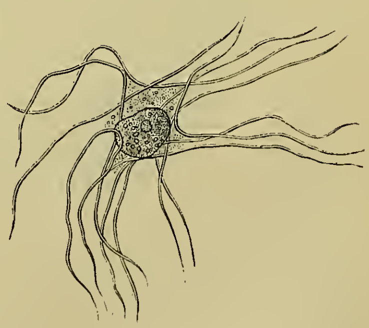


Fig. 377.—A neuroglia-cell from the cerebral cortex of the monkey, stained by Golgi's method (E. A. S.).

Fig. 378.—A neuroglia-cell, isolated in 33 p. c. alcohol (Ranvier).

radiating fibres to its periphery. Although these fibres become subsequently obscured by the great development of nerve-cells and fibres between them, it is probable that their remnants persist even in the fully developed condition of the nerve-centre.

Lastly, a certain amount of support is furnished to the soft matter of the central nervous system by the prolongations of pia mater (connective tissue sheath of the

brain and cord) which here and there dip in from the surface either as septa, such as that which passes into the posterior fissure of the spinal cord, or as carriers of blood-vessels, which everywhere enter the substance of the centro-spinal centre from the vessels of the pia mater.

CONSTRUCTION OF THE NERVES AND NERVE-ROOTS.

The nerves are formed of the nerve-fibres already described, collected together and bound up in sheaths of connective tissue. A variable number of fibres inclosed in a tubular sheath forms a slender round cord of no determinate size, usually named a *funiculus ;* if a nerve is small it may consist of but one such cord, but in larger nerves several funiculi are united together into one or more bundles, which, being wrapped up in a common membranous covering, constitute the nerve (fig. 379). Accordingly, in dissecting a nerve, we first come to an outward covering, formed of connective tissue, often so strong and dense that it might well be called fibrous. From this common sheath we trace connective tissue bundles passing between the funiculi, connecting them together as well as conducting and supporting the fine

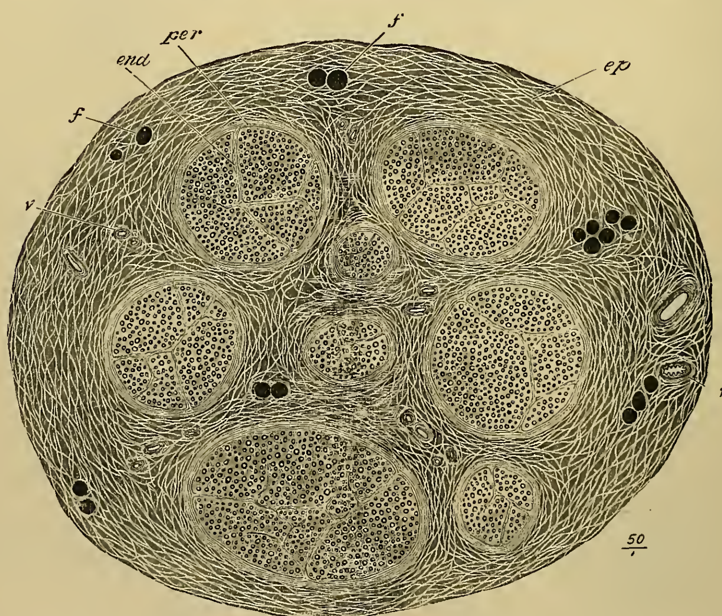


Fig. 379.—Section of the internal saphenous nerve (human), made after being stained in osmic acid and subsequently hardened in alcohol. Drawn as seen under a very low magnifying power. (E. A. S.)

ep, epineurium, or general sheath of the nerve, consisting of connective tissue bundles of variable size, separated by cleft-like areolæ, which appear as a network of clear lines, with here and there fat-cells *f f*, and blood-vessels *v* : *per*, funiculus enclosed in its lamellated connective tissue sheath (perineurium) ; *end*, interior of funiculus, showing the cut ends of the medullated nerve-fibres, which are embedded in the connective tissue within the funiculus (endoneurium). The fat-cells and the nerve-fibres are darkly stained by the osmic acid, but the connective tissue of the nerve is less stained.

blood-vessels which are distributed to the nerve. But, besides the interposed areolar tissue which connects these smallest cords, each funiculus has a special sheath of its own, as will be immediately noticed.

The common sheath (fig. 379, *ep*) and its sub-divisions consist of connective tissue with the usual white and elastic constituent fibres of that texture, the latter being present in considerable proportion : frequently also a little fat is to be found.

This common sheath has received the name of *epineurium* (Key and Retzius) ; it was formerly termed the "cellular sheath."

The special sheath of a funiculus, termed the *perineurium* [1] (fig. 379, *per*, 380, *P*.), is also formed of connective tissue, but is far more distinctly of a lamellar nature, and indeed may be stripped off in the form of a tube from the little bundle of nerve-fibres of which the funiculus consists. The perineurium is not formed of a single lamella but of several, which are separated from one another by inter-

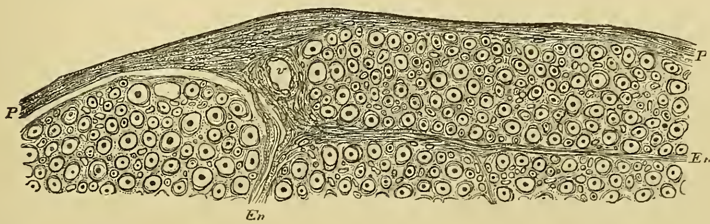


Fig. 380.—Part of a section of one of the funiculi of the sciatic nerve of man. Magnified (after Key and Retzius).

P, perineurium, consisting of a number of closely arranged lamellæ. *En*, processes from the perineurium, passing into the interior of the funiculus, and becoming continuous with the endoneurium, or delicate connective tissue between the nerve-fibres. The connective tissue fibrils of the endoneurium are seen cut across as fine points, often appearing to ensheath the nerve-fibres with a circle of minute dots (fibril-sheath of Key and Retzius). Numerous nuclei of connective tissue cells are imbedded in the endoneurium ; *v*, section of a blood-vessel.

lamellar clefts moistened with lymph. The separation is not everywhere complete, for here and there bundles pass across, connecting the several lamellæ. Moreover, the outermost lamella is joined by connective tissue bundles and laminæ of the

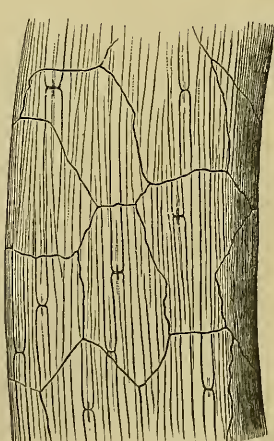


Fig. 381.—A portion of a small nerve-trunk from the thorax of a mouse, treated with nitrate of silver (Ranvier). Magnified.

Cross markings are seen at the nodes, and the layer of flattened epithelioid cells which covers the surface is brought into view by the silver deposit.

epineurium, and the innermost gives off flattened prolongations (fig. 379, *end*.), to form imperfect septa between the groups of nerve-fibres within the funiculus.

Although the lamellæ of the perineurium are very thin, each is formed of at least three strata. Thus the main substance of the lamella is composed of a connective tissue, in which both white fibres and elastic elements are found, the white fibres having for the most part a transverse disposition. The elastic elements lie in greater abundance nearer the surfaces of the lamella, and often occur in the form of patches or incomplete membranes of elastic substance (fig. 282, p. 240), as well as in the form of fine network of fibres. On both its surfaces each lamella is entirely covered with a layer of delicate flattened endothelial cells, which thus serve also to bound the clefts between the lamellæ. The outlines of the cells are brought into view by the silver treatment (fig. 381).

The funiculi of a nerve, although not all of one size, are all sufficiently large to

[1] Formerly known as the neurilemma.

be readily seen with the naked eye, and easily dissected out from each other. In a nerve so dissected into its component funiculi, it is seen that these do not run along the nerve as parallel insulated cords, but join together obliquely at short distances as they proceed in their course, the cords resulting from such union dividing in their further progress to form junctions again with collateral cords ; so that in fact the funiculi composing a single nervous trunk have an arrangement with respect to each other similar to that which is found to hold in a plexus formed by the branches of different nerves. It must be distinctly understood, however, that in these communications the medullated nerve-fibres do not join together or coalesce. They pass off from one nervous cord to enter another, with whose fibres they become intermixed, and part of them thus intermixed may again pass off to a third funiculus, or go through a series of funiculi and undergo still further intermixture ; but throughout all these successive associations the fibres remain individually distinct, like the threads in a rope.

The nerve-fibres are separated from one another, and supported within the funiculus by delicate connective tissue, the fibrils of which run for the most part longitudinally, appearing in section as fine points (fig. 380). This tissue has been distinguished as the *endoneurium* by Key and Retzius. It is continuous with the septa which pass in as above mentioned from the innermost lamella of the perineurium, and it serves to support also the capillary blood-vessels which are distributed to the nerve.

Lying alongside each other, the fibres of a funiculus form a little skein or bundle, which runs in a waving or serpentine manner within its sheath ; and the alternate lights and shadows caused by the successive bendings being seen through the sheath, give rise to the appearance of alternate light and dark cross stripes on the funiculi, or even on larger cords consisting of several funiculi. On stretching the nerve, the fibres are straightened and the striped appearance is lost. Both the perineurium and endoneurium accompany the nerves in all their divisions, in some cases as far as their peripheral terminations. In the finest branches the perineurium generally becomes reduced to a single connective tissue lamella, covered on both surfaces by endothelial cells. In this condition it is known as the *sheath of Henle.*

Both the cerebro-spinal and the sympathetic nerve-trunks are constructed in the manner above described, but the fibres of the cerebro-spinal nerves are chiefly of the white or medullated kind, and contain for the most part fibres of large size, while in nerves belonging to the sympathetic system non-medullated fibres or medullated fibres of very small size greatly preponderate. But very few nerves are composed exclusively of one or the other kind of fibre.

Vessels and Lymphatics.—The blood-vessels of a nerve after dividing into small branches in the epineurium and giving offsets to the groups of fat-vesicles which are there met with, pierce the layers of the perineurium obliquely, being supported by the connective tissue bundles which unite the lamellæ, and conducted into the interior of the funiculus along the septa before mentioned. Here they break up into fine capillaries which for the most part run parallel with the fibres, but are connected at intervals by short transverse branches, thus forming a network with long narrow meshes. Some of the capillaries may be observed to form loops. Lymphatic vessels are found in the epineurium, but within the funiculi there are no distinct vessels for the conveyance of lymph. It is found, however, that coloured fluid which is injected by means of a fine cannula into the interior of a funiculus finds its way into the lymphatics of the sheath after passing through the clefts between the lamellæ of the perineurium, so that undoubtedly a connection exists between these perineural clefts and the lymphatic system.

Course of the nerve-fibres in the nerve-trunks.—Neither in their course along the nervous cords, nor in the white part of the nerve-centres, do the

medullated fibres anastomose together, nor are they observed except in rare instances to divide into branches until they approach their termination. But the nerve-trunks themselves continually ramify, and the branches of different nerves not unfrequently join with one another. The branches are of course formed by collections of nerve-fibres, and it follows therefore that when two branches of nerves join, fibres pass from the one nerve-trunk to become associated with the other in their further progress, or the communication may be reciprocal, so that after the junction each nerve-trunk contains fibres derived from two originally distinct sources. In other cases the branches of a nerve, or branches derived from two or from several different nerves, are connected in a more complicated manner, and form what is termed a plexus. In plexuses—of which the one named "brachial" or "axillary," formed by the great nerves of the arm, and the "lumbar" and "sacral," formed by those of the lower limb and pelvis, are appropriate examples—the nerves or their branches join and divide again and again, interchanging and intermixing their fibres so thoroughly that, by the time a branch leaves the plexus it may contain fibres from several or even from all the nerves entering the plexus. Still, as in the more simple communications already spoken of, the fibres, so far as is known, remain individually distinct throughout.

In some instances of nervous conjunctions certain collections of fibres, after passing from one nerve to another, take a retrograde course in that second nerve, and, in place of being distributed peripherally with its branches, turn back to its root towards the cerebro-spinal centre. Instances of this occur, according to Volkmann, in the connection between the second and third cervical nerves of the cat, in that of the fourth cranial nerve with the first branch of the fifth, and of the cervical nerves with the spinal accessory and the descending branch of the hypoglossal.

Origins or roots of the nerves.—The cerebro-spinal nerves, as already said, are connected by one extremity to the brain or to the spinal cord, and this central extremity of a nerve is, in the language of anatomy, named its origin or root. In

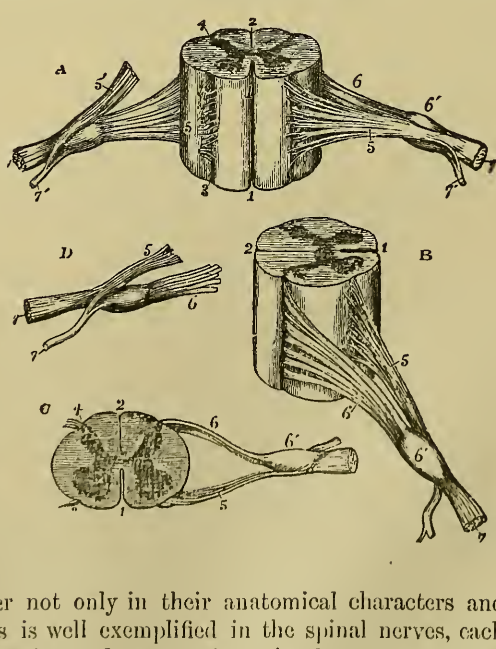


Fig. 382.—Roots of one of the spinal nerves issuing from the spinal cord. (Allen Thomson.)

A, from before; B, from the side; C, from above; D, the roots separated; 5, 5, anterior root; 6, 6, posterior root with ganglion, 6′. The full description of this figure will be found in the chapter on the cerebro-spinal nervous axis.

some cases the root is single, that is, the funiculi or fibres by which the nerve arises, are all attached at one spot or along one line or tract; in other nerves, on the contrary, they form two or more separate collections, which arise apart from each other and are connected with different parts of the nervous centre, and such nerves are accordingly said to have two or more origins or roots. In the latter case, moreover, the different roots of a nerve may differ not only in their anatomical characters and connections, but also in function, as is well exemplified in the spinal nerves, each of which arises by two roots, an anterior and a posterior—the former containing the efferent fibres of the nerve, the latter the afferent.

The fibres of a nerve may be traced to some depth in the substance of the brain or spinal cord, and hence the term "apparent or superficial origin" has been employed to denote the place where the root of a nerve is attached to the surface, in order to distinguish it from the "real or deep origin" which is beneath the surface and concealed from view. If the deep origin be traced out, it will usually be found that the nerve-fibres arise from portions of the grey substance of the nerve-centre: such a portion of grey substance is termed the "nucleus of origin" of the nerve.

In the case of the efferent nerves it would appear that the individual nerve-fibres originate as prolongations of the nerve-cells in the grey substance. In fact, as the researches of His have shown, these nerve-fibres have grown out from the nerve-cells (neuroblasts) within the embryonic nerve-centre (see Embryology, Development of

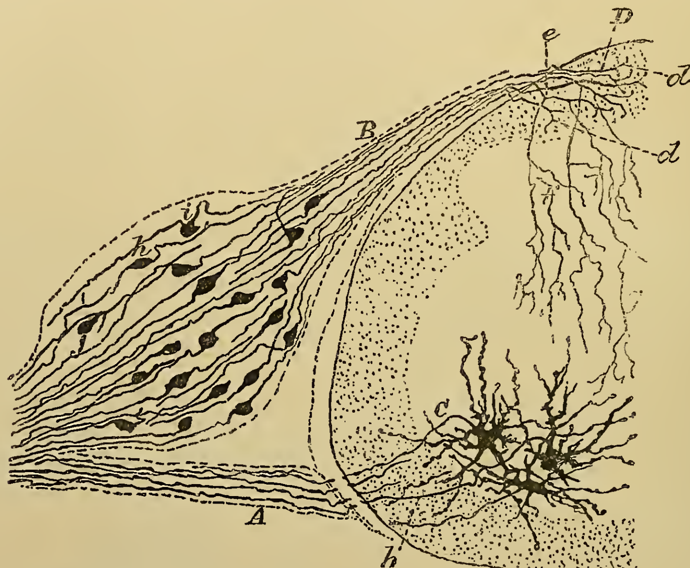


Fig. 383.—Transverse section of the spinal cord of a chick on the 9th day of incubation, prepared by Golgi's method (Ramón y Cajal).

A. Axis-cylinders of anterior root-fibres issuing from large cells of the anterior cornu, C.

B. Posterior root-fibres passing from the bi-polar cells of the spinal ganglion, E, into the posterior column of the spinal cord (D), where they bifurcate (*d*) and become longitudinal.

e, f, g, collateral branches from these fibres, passing into the grey matter.

Nerves). In the case of afferent nerves it seems to be clear that these in most if not all cases have grown *into* the nerve-centre from the cells of the ganglia, or from nerve-cells in the peripheral organs of special sense. Having entered the nerve-centre (fig. 383, D) the afferent fibres appear usually to bifurcate—at least this is the case with the fibres of the posterior spinal roots—and the two resulting branches become longitudinal, sending off lateral ramuscles (*e, f, g*) into the grey matter, in which they appear to break up into fine ramifications, without being directly continuous with nerve-cells of the grey substance.

In the nerve-roots the fibres are bound up together, as they pass towards the foramina of exit from the cranio-vertebral canal, by a stout external sheath continuous with the pia mater and receiving an accession from the arachnoid and dura mater as the roots pass through those membranes. This sheath sends in strong septa which branch and unite with one another in the nerve-root, and thus divide it up irregularly into bundles of fibres, which have not the same cylindrical character, with special lamellated sheaths of perineurium, as the funiculi of the peripheral nerves,

but are supported by a kind of framework formed by the dividing septa above mentioned. Only after passing the ganglia do the nerves acquire a true funiculated structure such as has been described for the peripheral nerves. The optic nerve has throughout its whole course the structure of a nerve-root.

The cerebro-spinal nerve-trunks and their branches always present a brilliant whitish aspect, whereas the sympathetic nerves vary in appearance, some being whiter, others grey or reddish in colour. The more grey-looking branches or bundles consist of a large number of the pale fibres mixed with a few of the medullated kind ; the whiter cords, on the other hand, contain a proportionally large amount of

A B C D

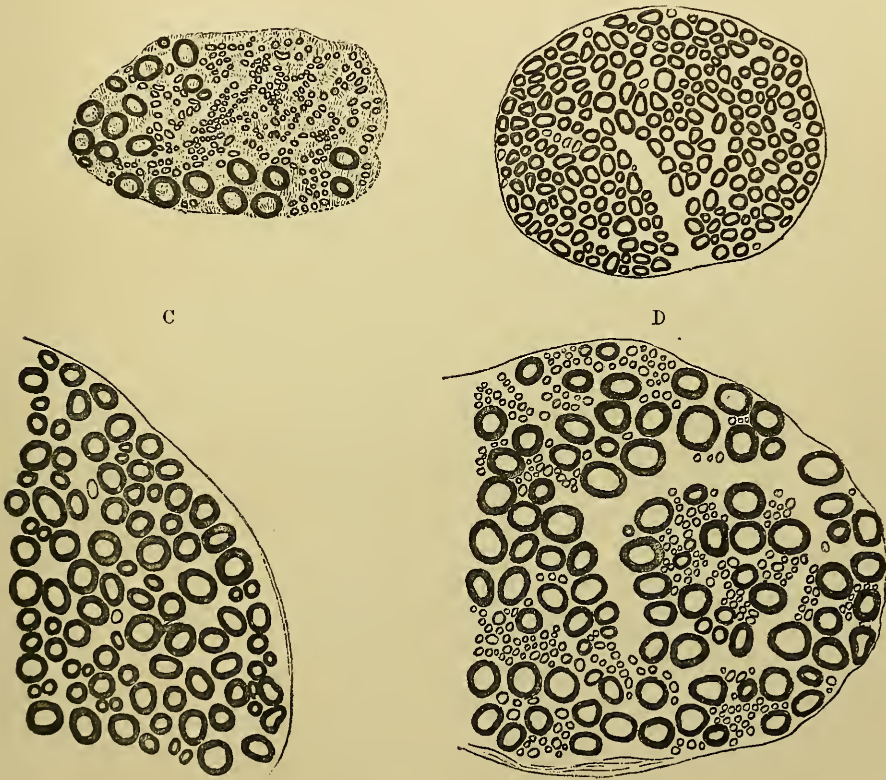


Fig. 384.—Sections across parts of the roots of various nerves of the dog, to show the variations in size of their constituent fibres (Gaskell).

The nerves were stained with osmic acid, and the sections are all drawn to one scale.
A, from one of the upper roots of the spinal accessory.
B, a rootlet of the hypoglossal.
C, from the 1st cervical anterior root.
D, from the 2nd thoracic anterior root.

fine medullated fibres, and fewer of the grey ; and in some parts of the nerve grey fasciculi and white fasciculi, respectively constituted as above described, run alongside of each other in the same cords for a considerable space without mixing. This arrangement may be seen in some of the branches of communication with the spinal nerves, in the trunk or cord which connects together the principal chain of sympathetic ganglia, and in the primary branches proceeding thence to the viscera. In the last-mentioned case the different fasciculi get more mixed as they advance,

but generally it is only after the white fasciculi have passed through one or more ganglia that they become thoroughly blended with the grey; and then, too, the nervous cords receive a large accession of grey fibres, while the white fibres are reduced in number.

Differences are observed among the cerebro-spinal nerves in the proportionate amount of the two kinds of fibres which they respectively contain, and in the size of their white fibres. Volkmann and Bidder showed that nerves going to voluntary muscles have very few small fibres, those going to the integuments a large proportion of small fibres, whereas those distributed to involuntary muscles and to the viscera have many more small fibres than large. The circumstances influencing these variations were not, however, understood until it was shown by Gaskell that the very fine medullated fibres pass out from the cerebro-spinal axis in certain regions only, and are distributed exclusively to the viscera and blood-vessels, for the

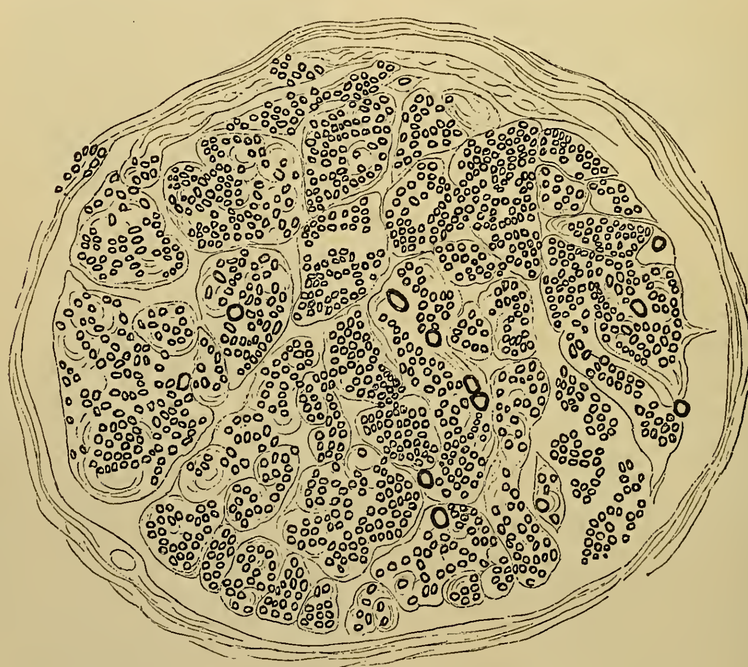


Fig. 385.—Section of a white ramus communicans from the dog (Gaskell).

The section is drawn to the same scale as those shown in fig. 382, and the nerve-fibres are stained by osmic acid.

most part through the sympathetic system, but partly directly through the cerebro-spinal nerves. In the cranio-cervical region these small fibres pass out with the upper roots of the spinal accessory nerve and partly perhaps with those of the vagus, glosso-pharyngeal and facial; in the thoracico-lumbar region with the anterior roots of the nerves from the second thoracic to the second lumbar inclusive, and in the sacral region with the anterior roots of the second, third, and perhaps the fourth sacral nerves.

These fine medullated fibres form the only true communication between the cerebro-spinal centre and the sympathetic, and, in fact, those of the dorso-lumbar outflow give origin to the main sympathetic system. Passing to the nearer ganglia of the sympathetic, many of them lose their medullary sheath on joining with the cells of those ganglia, and are continued as pale fibres: others

pass through the nearer ganglia without joining the nerve-cells and are continued towards their peripheral distribution as fine medullated fibres, but lose their medullary sheath in passing through distal ganglia of the sympathetic system. It has further been shown by Gaskell that there is a functional difference between these two kinds of fibres, those at least which are distributed to the bloodvessels, for whereas the fibres which early lose their medullary sheath produce increased contraction of the muscular coat, the others produce diminished contraction or inhibition. Amongst the nerves stimulation of which produces inhibition of contraction, that which has been longest known is the cervical part of the vagus which sends branches to the cardiac plexus, and to the heart. This nerve is found to contain a large number of fine medullated fibres, which for the most part reach it from the upper roots of the spinal accessory.

The proportion of fine medullated nerve-fibres which the roots of the cerebro-spinal nerves contain may be taken as a direct indication of the extent to which they feed the sympathetic system. This is at least true for the region of the thoracic outflow of vascular and visceral nerves. All the anterior roots in this region contain a large number of fine medullated fibres which leave the root in a bundle and pass directly to the sympathetic chain forming the white *ramus communicans* (fig. 385) between the spinal root and the sympathetic (Gaskell has shown that the so-called "grey ramus communicans" is in all cases merely a branch from the sympathetic to the bloodvessels of the spinal cord and of the nerve-roots). A section therefore through one of these anterior roots taken before the white ramus leaves it shows a large number of fine medullated fibres intermingled with the ordinary large fibres of the root, and contrasts forcibly with a section across one of the anterior roots of other regions where there is no sympathetic outflow, and, therefore, no white ramus communicans, and few, if any, fine medullated fibres. (Compare fig. 384, C and D.)

The bearing of these facts upon the morphology of the cerebro-spinal nerves and of the sympathetic will be dealt with in the part of this work which treats of the anatomy of the nervous system (Neurology).

CONSTRUCTION OF THE GANGLIA.

Situation.—Ganglia are found in the following situations—viz.: 1. On the posterior root of each of the spinal nerves; on the corresponding root of the fifth cranial nerve; on the facial, auditory, glosso-pharyngeal and pneumogastric nerves. 2. In a series along each side of the vertebral column, connected by nervous cords, and constituting what is known as the trunk of the sympathetic. 3. On branches of nerves, especially of the sympathetic; occurring numerously in the abdomen, thorax, neck, and head; generally in the midst of plexuses, or at the point of union of two or more branches. Those which are found in several of the fossæ of the cranium and face are for the most part placed at the junction of fine branches of the sympathetic with branches, usually larger, of the cerebro-spinal nerves.

The roots of certain of the cranial nerves, which do not exhibit true ganglia, such as the 3rd and 6th, have been shown by Thomsen and by Gaskell to possess what appear to be the remains of atrophied ganglion cells in the form of masses of granular material lying between the nerve-fibres, and devoid of all cellular structure. According to Hale White some of the sympathetic ganglia in man also show signs of atrophy of many of their cells in the adult.

The ganglia differ widely from each other in figure and size: most of those which have been longest known to anatomists are conspicuous objects; but there are numerous small or microscopic ganglia disposed along the branches of nerves distributed to the heart, the lungs, and other viscera; and also connected with fine plexuses of nerves between the coats of the stomach and intestines.

Structure.—Ganglia are invested externally with a thin, but firm and closely

adherent covering of connective tissue : this outward covering sends processes inwards through the interior. A section carried through a ganglion in the direction of the nervous cords connected with it, discloses collections of nerve-cells, between which the nerve-fibres pass (fig. 386). Each cell is inclosed in a transparent capsule with nuclei upon its inner surface (figs. 366, 367) ; these capsules are continuous with the primitive sheaths of the nerves (M. Schultze).

Of the relation between the nerve-fibres in a ganglion and the ganglion-cells, it is probable that some fibres may pass through without being connected with the cells, but that every nerve-cell is connected with a fibre or with fibres. In the case

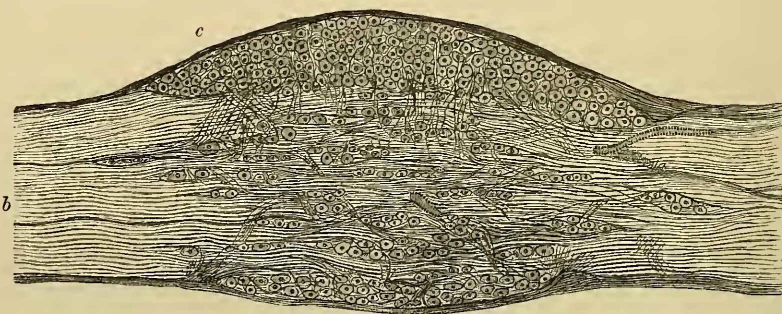


Fig. 386.—Longitudinal section through the middle of a ganglion on the posterior root of one of the sacral nerves of the dog, as seen under a low magnifying power. (E. A. S.)

a, Nerve-root entering the ganglion ; *b*, fibres leaving the ganglion to join the mixed spinal nerve ; *c*, connective tissue coat of the ganglion ; *d*, principal group of nerve-cells, with fibres passing down from amongst the cells, probably to unite with the longitudinally coursing nerve-fibres by T-shaped junctions (see text).

of multi-polar cells, such as are found in the sympathetic ganglia (fig. 367), each of the branches of the cell is in all probability continuous with a nerve-fibre, and the same is certainly the case with bipolar cells, at least those in which the two poles are prolonged from opposite extremities of the cell as in the spinal ganglia of fish (fig. 370), as well as in the pyriform cells before noticed (see p. 318) in which two processes arise from a part of the cell near one another, and are continued in

Fig. 387.—Bipolar cell from spinal ganglion of a $4\frac{1}{2}$ weeks' human embryo (His).

opposite directions, either at once, or after the one fibre has made two or more spiral coils around the other or straight fibre. Uni-polar cells are found in the spinal ganglia of the higher vertebrates (fig. 366). In them the single nerve-fibre process is observed to divide before long into two fibres (*d*), which traced far enough are found to pass in opposite directions toward the ends of the ganglion. Sometimes the branches are of equal size, but they are often unequal, one being decidedly smaller than the other. As in all cases of a division of a medullated nerve-fibre, the bifurcation takes place at a node of Ranvier, and this may be the first node from the cell, or the nerve-fibre may pass two or three or more nodes before thus dividing. The cell-process, which usually acquires its medullary sheath very soon

after leaving the cell, is often convoluted over the surface of or around the cell; this is especially the case in the human spinal ganglia. Its bifurcation, or in other words its junction with a nerve-fibre traversing the ganglion is often T-shaped.

These T-shaped divisions were first noticed by Ranvier. They have been found by Retzius in the spinal ganglia of all classes of vertebrates above fishes—where the cells are bipolar like that shown in fig. 370; and also in man, in the spinal ganglia, in the jugular and cervical ganglia of the vagus, the geniculate ganglion of the facial and the Gasserian ganglion of the trigeminal; but not in the otic, the spheno-palatine, the sub-maxillary and the ciliary ganglion, the cells of all of which are multi-polar, and hence resemble those which are found in the sympathetic.

Cells which are transitional in character between the bipolar cells of most fishes and the unipolar cells with forked process of the higher vertebrates, occur, as Freud has shown, in Petromyzon, in which, in addition to the ordinary bipolar cells, some of the cells have their two processes coming off quite close to one another, and others are unipolar with a short single process which soon bifurcates to form two nerve-fibres passing in opposite directions.

In the embryo the cells of the spinal ganglia are at first spindle-shaped and bipolar (fig. 383. *h*, *i*, fig. 387), with one process growing into the spinal cord and the other into the peripheral nerve. Gradually the processes approach one another and eventually come off from the cell by a common stalk (His).

Termination, or Peripheral Distribution, of Nerves.

It may be stated, generally, and apart from what may apply to special modes of termination, that, in approaching their final distribution, the fibres, medullated and

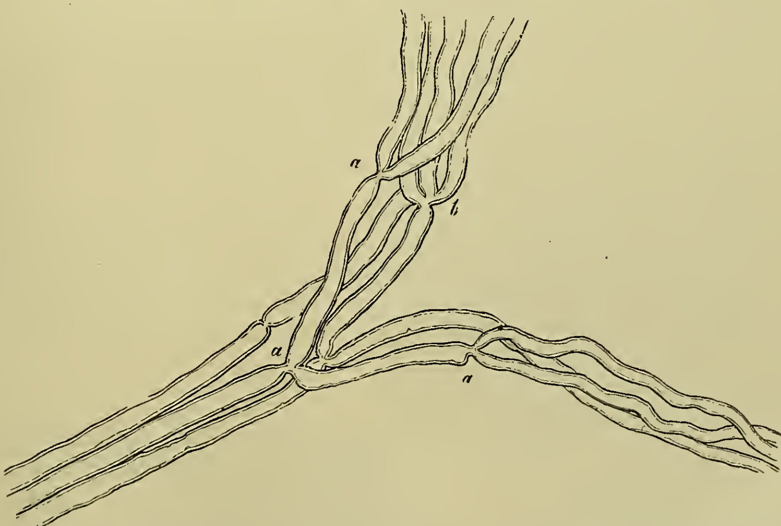


Fig. 388.—Small branch of a muscular nerve of the frog, near its termination, showing divisions of the fibres. Magnified 350 diameters (Kölliker).
a, into two; *b*, into three.

non-medullated, usually divide into branches, the division in the case of medullated fibres always occurring in the situation of a node of Ranvier (fig. 388). The axis cylinder participates in the division; and since the white fibres frequently lose their medullary sheath shortly before they terminate, they are then represented by the axis-cylinder and its ramifications, although the primitive sheath may continue some little way along the branches after the medullary sheath has ceased. By repeated

division the fibres usually become smaller ; but whilst some of the resulting small fibres may be simple, many are really bundles of fine fibrils.

These pale fibres bear nuclei, which probably appertain to the prolongation of the primitive sheath ; the nuclei are common at the bifurcations of the fibres, where they are of a triangular or irregular shape. The original dark-bordered fibres which thus undergo division and change, or which may proceed singly to end in a different and special manner, are commonly provided with a tolerably strong connective tissue sheath with nuclei, which, as it stands well apart from the dark borders of the fibre, is very conspicuous (sheath of Henle). This is derived from the perineurium which incloses the funiculi of the nerve-trunks, and, as these part into smaller collections and single fibres, undergoes a corresponding division, and finally sends sheaths along single fibres. Within the sheath of Henle fine longitudinal connective tissue fibres, with interspersed corpuscles, are seen surrounding the nerve-fibre or fibres. This tissue is a prolongation of the endoneurium.

In further treating of the termination of nerves, it will be convenient to consider the sensory and motor nerves separately.

TERMINATION OF SENSORY NERVES.

The sensory or afferent nerves end either in cells or in free nerve-endings, which may be simple or plexiform, and may be enclosed by cells or have an independent distribution. Of the sensory nerves which terminate in cells, the best recognised are those which are found in the organs of special sense. But these nerves may perhaps be regarded as taking origin in the sense-organ rather than ending in it, for if their development is studied it would appear, at least in the case of the olfactory and visual organs, that the nerve-fibres grow *from* the sense-organ towards the central nervous system and not centrifugally, as is the case with most other nerve-fibres. Their mode of connexion with the cellular elements of the special sense-organs will be studied most conveniently when those organs are themselves treated of.

Of the ordinary sensory nerves, including those which are devoted to the perception of tactile sensations, some end in ramifications of the axis cylinder, which resolves itself eventually into its ultimate fibrils, and thus penetrates between the epithelium-cells which cover the sensory surface, whilst others terminate in special organs, of which the best known are the *tactile corpuscles*, *simple and compound end-bulbs*, the *corpuscles of Grandry*, which occur in birds, the *round end-bulbs* of the human conjunctiva, *cylindrical end-bulbs*, *corpuscles of Herbst*, also occurring in birds, and the *corpuscles of Vater* or *Pacinian bodies*.

A B

Fig. 389.—A. Two tactile cells in the deeper part of the human epidermis. (Merkel.)
B. Ending of nerves in tactile disks in the pig's snout. (Ranvier.)

n, nerve-fibre ; *m*, terminal menisci or tactile disks ; *e*, ordinary epithelium-cell ; *a*, altered epithelium cell, to which the meniscus is applied.

Tactile cells (Merkel). Tactile cells, isolated or in groups, but in the latter case not collected together to form a tactile end-organ, were described by Merkel as occurring in the deeper layers of the epidermis and sometimes in the subjacent true skin over almost the whole of the body (fig. 389 A). In animals they are especially numerous in parts of the skin which are devoid of hairs, as in that which covers the soles of the feet, and on the snout, as well as amongst the epithelium-cells of the hard palate. The cells in question are round or pyriform in shape, and prolonged at one part into the axis-cylinder of a nerve-fibre: in cases where the axis-cylinder is ramified, it may be connected with more than one of these cells. Each cell is stated to be inclosed by a cell-membrane which is continuous with a prolongation of the primitive sheath of the nerve-fibres. When the tactile cells occur in the superficial layers of the cutis vera instead of amongst the cells of the epidermis they are found to be enclosed in a capsule of connective tissue, which is pierced by the axis-cylinder of the nerve-fibre as this passes to apply itself to one of the surfaces of the usually flattened cell. Such a cell, inclosed in a capsule and forming the termination of a nerve-fibre, represents, according to Merkel, the tactile end-organ in its simplest form. The existence of tactile cells such as are described by Merkel is, however, not generally admitted by histologists, but Ranvier has described and figured a mode of termination which is somewhat like that described by Merkel with the exception that the nerve-fibres do not pass directly into the cells, but come into connexion with them through the medium of concavo-convex expansions, to which he has given the name of *tactile disks* or *menisci* (fig. 389 B). Haycraft states that in the carapace of the tortoise the nerves end in the nuclei of some of the deeper cells of the epidermis.

Tactile corpuscles or touch-bodies (*corpuscula tactûs*)—(figs. 390 to 393). These were discovered by R. Wagner and Meissner in the papillæ of the skin of the hand and foot, where they are of an oval shape, nearly $\frac{1}{300}$ of an inch long and $\frac{1}{800}$ of an inch thick. They may be found in the skin of all parts of the hand and foot, including the bed of the nails, that of the volar surface of the forearm, in the skin of the nipple in both sexes, in the conjunctiva at the edge of the eyelids, and in the skin of the lips and in the mucous membrane of the tip of the tongue. Similar corpuscles occur in monkeys, but have not been found in animals lower in the scale. One, two, or more medullated nerve-fibres run to the corpuscle and either at once or after winding round it two or more times, pass into its interior and become lost to view. The tactile corpuscles were long described as consisting of a soft structureless core or central part, in which the nerve-fibres were thought to terminate by bulbous enlargements, and of an inclosing capsule of connective tissue, continuous with the perineurium of the nerve, and composed for the most part of transverse or spiral fibres and nuclei, so arranged as to give the little body somewhat the aspect of a miniature fir-cone. It would appear however that a core, like that of the Pacinian corpuscles to be presently described, does not in reality exist in these corpuscles, but that the main substance of the touch-body is composed of connective tissue, prolonged inwards from the capsule in the

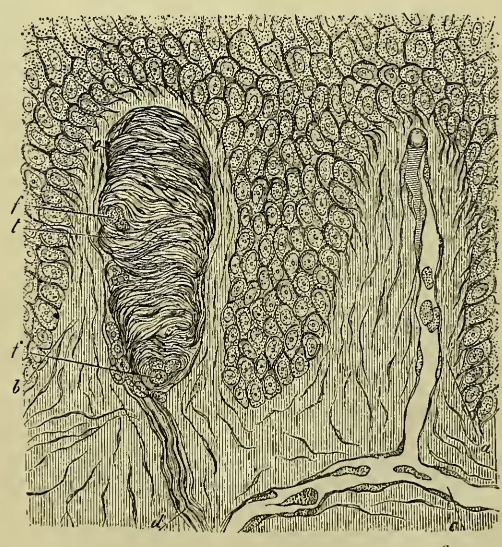


Fig. 390.—SECTION OF SKIN SHOWING TWO PAPILLÆ AND DEEPER LAYERS OF EPIDERMIS. (Biesiadecki.)

a, vascular papilla with capillary loop passing from subjacent vessel, *c*; *b*, nerve-papilla with tactile corpuscle, *t*. The latter exhibits transverse fibrous markings: three nerve-fibres, *d*, are represented as passing up to it: at *f f* these are seen in optical section.

form of imperfect membranous septa (figs. 392, 393 A), between which are supported the convolutions and ramifications of the nerves, and the enlargements in which the branches of the axis-cylinder eventually end (small tactile cells according to Merkel). These terminal enlargements, which are either pyriform or globular in shape, are always placed near the capsule, and in small tactile corpuscles may occasionally project beyond it. On entering the corpuscle the nerve-fibres for the most part lose

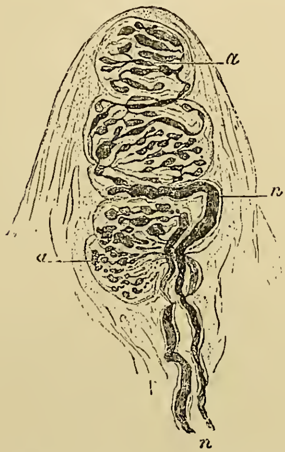


Fig. 391. — Tactile corpuscle within a papilla of the skin of the hand, stained with chloride of gold. Highly magnified. (Ranvier.)

n, *n*, two nerve-fibres passing to the corpuscle ; *a*, *a*, terminal, varicose ramifications of the axis-cylinder within the corpuscle.

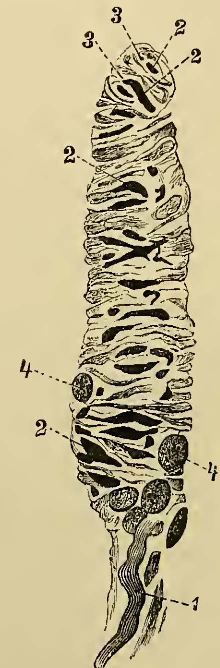


Fig. 392.—Another corpuscle, treated with osmic acid, seen in longitudinal section. (Flemming, from a preparation by Fischer.)

1, entering nerve-fibre, medullated ; 2, 2, the same cut variously within the corpuscle ; 3, 3, clear spaces around the fibre (perhaps homologous with the core of the cylindrical end bulbs) ; 4, 4, nuclei of the transverse and spirally-disposed cells of the corpuscle.

Fig. 393.—Tactile corpuscles from the palm of the hand, seen in section (Merkel).

A, Longitudinal section showing the interior traversed by connective tissue septa derived from the capsule ; the nerve-fibres are cut across. B, transverse section at the point of entrance of a nerve-fibre, showing the axis-cylinder branching. Other nerve-fibres are cut obliquely.

their medullary sheath, but some retain it for a short while, or it may reappear here and there in the course of the fibres. The axis-cylinders, which are often varicose, have, as before intimated, a convoluted course before ending in their terminal enlargements (fig. 391).

The absence of a central core such as is found in the Pacinian corpuscles, and in some end-bulbs, was first pointed out by Langerhans and afterwards by Thin. The latter observer stated as the result of his observations, that tactile corpuscles could be divided into simple or compound, according as they receive one or a greater number of nerve-fibres ; each nerve-fibre passing to one distinct corpuscle, and the larger corpuscles being compounded of two or more simple ones. On the other hand, even in the same papilla, several small corpuscles may occur near to but distinct from one another.

End-bulbs.—If the conjunctiva of the calf or of certain other animals is carefully spread out and examined under the microscope, many of the medullated nerves which course in different directions in the membrane may be seen to end in very small oval or elongated corpuscles, into the interior of which the axis-cylinder of the nerve-fibre passes, surrounded by a soft homogeneous core, to end near the extremity of the corpuscle, with a rounded or dilated termination. The core with its contained fibre is inclosed in a simple nucleated capsule composed of flattened cells. The medullary sheath ceases abruptly at the entrance of the nerve, whereas the primitive sheath appears to be continued over the core, and to line the capsule. These

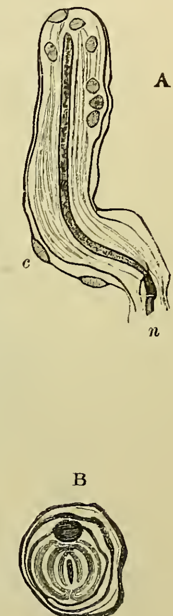


Fig. 394.—Cylindrical end-bulbs from the conjunctiva of the calf. (Merkel.)

A, in optical longitudinal section ; B, in transverse section ; *n*, entering nerve-fibre ; *c*, nucleated capsule.

so-called *cylindrical end-bulbs* were discovered by W. Krause, and they have been found not only in the conjunctiva of different mammals, but also forming the most common mode of nerve-termination in various parts of the skin and here and there in the mucous membrane of the mouth. Terminal corpuscles of this exact nature and form, have however hitherto not been observed in the conjunctiva of man nor of apes, but their place is here supplied by the small *spheroidal end-bulbs* of Krause (figs. 395, 396), which have also been found in man in the papillæ of the skin covering the lips, in the mucous membrane of the cheeks, soft palate, tongue, epiglottis, nasal cavities, lower end of the rectum, and in that of the glans penis and clitoridis. Corpuscles which are closely allied to, if not identical with these, are also found in the epineurium of nerve trunks, where they constitute the terminations of the *nervi nervorum* (Horsley). The spheroidal end-bulbs (fig. 395, B, C) are composed of a connective tissue capsule (*a*) inclosing a core formed of numbers of polygonal and elongated cells, which give the core a granular aspect ; amongst the cells of the core the axis-cylinder terminates. Sometimes the small medullated fibre which passes to each spheroidal end-bulb, divides into two or more branches before reaching the bulb, and the branches may be twisted around one another on their passage towards the organ (B). The capsule is continuous with the sheath of Henle of the nerve-fibre, and internally it is closely invested with a nucleated membrane, prolonged from the primitive sheath. Like the tactile corpuscles, spheroidal end-bulbs have not been noticed in any animals below monkeys.

The cylindrical end-bulbs closely resemble the central part or core of a Pacinian body divested of all but its innermost tunic, and, to complete the resemblance, flattened concentrically arranged cells are described by Merkel as forming the core of the end-bulb as well as that of the Pacinian. In short, it would seem as if the little bodies in question represent the simplest of the type of terminal corpuscles of which the Pacinian corpuscles are the most complex examples ; the complexity having been produced in the latter by the multiplication of the tunics. In conformity with this view it may be mentioned that corpuscles resembling the Pacinian bodies are frequently found, especially in the lower animals, in which the tunics are few in number and the corpuscles correspondingly smaller. On the other hand, the round end-bulbs approach more nearly to some of the tactile corpuscles in structure, those, namely, of a simple kind, such as are met with in many parts of the integument, and those form a transition to the more complicated tactile corpuscles which occur in the papillæ of the human hand. At the same time it cannot be supposed that there is any fundamental difference in the two kinds of end-bulb, although the arrangement of the cells in the core and the course taken by the

nerve-fibre is somewhat different, since we see that in different animals those of the one kind are replaced by those of the other kind.

Large end-bulbs of a rounded oval form have been found in the synovial membrane of certain joints in man (*e.g.*, those of the fingers), and also in the

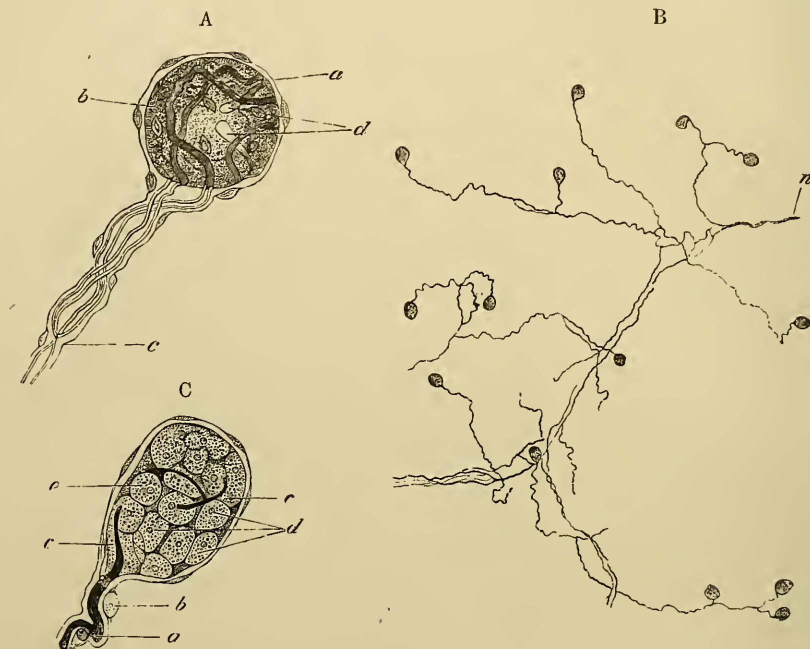


Fig. 395.—END-BULBS FROM THE HUMAN CONJUNCTIVA. (Longworth.)

A, Ramification of nerve-fibres in the mucous membrane, and their termination in end-bulbs, as seen with a lens ; B, an end-bulb more highly magnified ; *a*, nucleated capsule ; *b*, core, the outlines of its component cells are not seen ; *c*, entering fibre branching and its two divisions passing to terminate in the core at *d* ; C, an end-bulb treated with osmic acid, showing the cells of the core better than B ; *a*, the entering nerve-fibre ; *b*, capsule with nuclei ; *c*, *c*, portions of the nerve-fibre within the end-bulb, the ending of the fibre is not seen ; *d*, *e*, cells of the core.

articular synovial membranes of several mammals. They are somewhat flattened, have a large granular core beset with nuclei, and receive from one to four medullated nerve-fibres, which terminate within them in fine convoluted and ramified non-medullated filaments (fig. 397). They are distinguished by the name of *articular nerve-corpuscles* or *articular end-bulbs.*

What appear to be a modification of end-bulbs were discovered by W. Krause in certain parts of the external generative organs, both in the male and female (especially the glans penis and clitoridis), and were named by him *genital corpuscles.* These corpuscles are constructed generally like the end-bulbs, but are characteristically constricted or subdivided by connective tissue septa into from two to six knob-like portions, which gives the whole corpuscle a mulberry-like aspect. From one to four medullated fibres enter the genital corpuscle, and their axis-cylinders usually break up within it into a large number of fine pale terminal fibres. Their size varies greatly, some of them being no larger than ordinary end-bulbs, others several times as large. In the simplest of these structures the axis-cylinder of the nerve-fibre entering at one pole of the somewhat oval corpuscle (fig. 398) may either pass straight or with

one or two bendings through the corpuscle, and end by a tapering (A) or by a dilated extremity (B) near the opposite pole (often projecting beyond the general body of the organ, as in B); or it may be much convoluted and ramified in its passage,

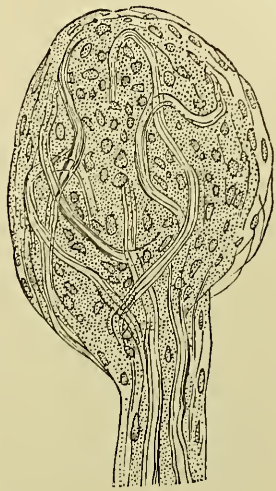


Fig. 396.—End-bulb of the human conjunctiva, treated with 3 p.c. acetic acid and 1 p.c. osmic acid. $\frac{500}{1}$. (W. Krause.)

Fig. 397.—Articular corpuscle from phalangeal joint in man. Acetic acid preparation. (W. Krause.) $\frac{300}{1}$.

n, two medullated nerve-fibres entering the corpuscle.

so as to render it a matter of difficulty to trace its course and mode of termination (fig. 398 C). The arrangement of the cells in these corpuscles seems to vary considerably. Sometimes they are chiefly collected at the exterior, leaving the part

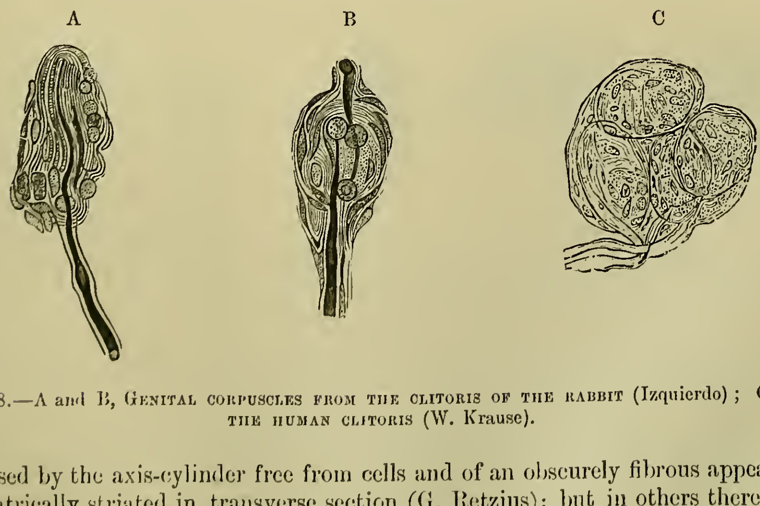


Fig. 398.—A and B, Genital corpuscles from the clitoris of the rabbit (Izquierdo); C, from the human clitoris (W. Krause).

traversed by the axis-cylinder free from cells and of an obscurely fibrous appearance, concentrically striated in transverse section (G. Retzius); but in others there is an agglomeration of cells in the centre, as in the spheroidal end-bulbs of the human conjunctiva; this is, however, denied by Retzius.

Tactile end-organs of birds.—On account of the light which they throw upon the structure of the end-bulbs of mammals, a short description of the tactile end-organs of birds may be given here.

It was noticed by Grandry that in the soft skin covering the bill of certain birds, such as the duck and goose, a peculiar form of end-organ exists consisting of two or more flattened cells, inclosed in a common capsule of connective tissue, and receiving between them the termination of the axis-cylinder (fig. 399). The structures in question have since been investigated by several observers with the following results:—

The cells which form the corpuscle of Grandry are for the most part of no great thickness, and the surfaces which are opposed to one another are flattened. Their protoplasm is stated by Merkel to resemble that of nerve-cells, having a striated aspect, the striæ being partly concentric with the periphery of the cell, partly passing radially through it. The nucleus has also been compared to that of a ganglion-cell. There may be two only of these cells (which are termed by Merkel "tactile cells," by others "protective or inclosing cells") in a corpuscle of Grandry, or there may be three or four or even more, piled the one on the other. When numerous they may lose their regularity of arrangement. Occupying the interval between every two cells is a flattened disk termed the "tactile disk," and according to the testimony of all observers the axis-cylinder of the entering nerve-fibre ends in these tactile disks. According to Merkel, the disk is itself, on the other hand, directly in continuity with one or both of the cells between which it lies, but this continuity is not generally admitted. The tactile cells and disks are all inclosed in a common capsule or sheath of connective tissue continuous with the perineurium of the nerve and receiving also a lining from the nucleated sheath of Schwann. From the capsule incomplete septa pass inwards between the flattened cells, as far as the edges of the tactile disks, so that the septa look as if they were perforated to receive the disks. Usually a single nerve-fibre passes to each corpuscle, and this may either lose its medullary sheath on entering the corpuscle or may retain it for some part of its course, although it eventually, in any case, becomes lost. The axis-cylinder, passing between the capsule and the tactile cells, divides into as many branches as there are tactile disks, in which, as already mentioned, it finally terminates.

It will appear from the above account that the chief point in which there is a difference of opinion with regard to the structure of the simply constructed tactile corpuscles, is as to the expansion of the axis-cylinder known as the tactile disk, whether this is prolonged or not into the cells which cover it. The former view is taken, as we have seen, by Merkel, but the opinions of most other observers are adverse to it. There is, however, this to be said in favour of Merkel's view, namely, that when degeneration takes place as a result of the section of the nerve, the degenerative process extends not only to the tactile disk but also to the cells which cover it.

These corpuscles appear to be developed as a result of the multiplication and down-growth of some of the epithelium-cells which lie at the apex of a papilla (fig. 399, C). The growth be-

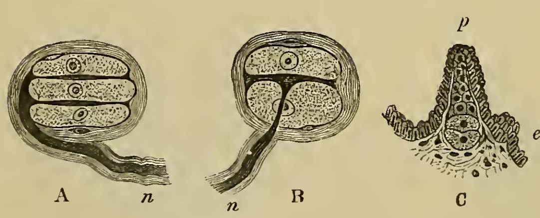


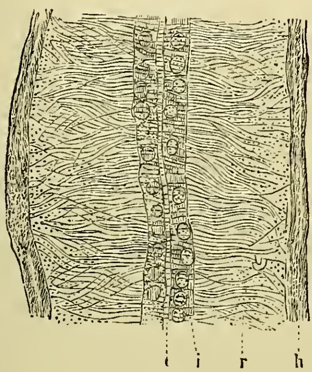
Fig. 399.—Tactile corpuscles from the duck's tongue. (Izquierdo.)

A, composed of three cells, with two interposed disks, into which the axis-cylinder of the nerve, *n*, is observed to pass; in B there is but one tactile disk enclosed between two tactile cells; C illustrates the development of a tactile corpuscle like the one shown in B; *e*, deeper cells of the epithelium covering the papillated surface of the tongue; *p*, apex of a papilla, in which there is seen to be a downgrowth of epithelium-cells, the lowermost of which are developed into tactile cells.

comes entirely cut off from the rest of the epithelium and surrounded by connective tissue, whilst the cells within it are converted into the flattened "tactile cells," and a prolongation of a nerve-fibre grows up into it.

Corpuscles of Herbst (fig. 400).—These, which form the principal mode of nerve-termination in the bird's skin, are in structure similar to large cylindrical end-bulbs. They have a core consisting of nucleated cells, which are disposed transversely, and through the middle of which the axis-cylinder passes. Their capsule is composed of an outer longitudinal fibrous tissue, and an inner layer of strongly-marked fibres of a brownish colour, running transversely or circularly. They most nearly resemble the innermost part of the Pacinian corpuscles, *i.e.*, the core and the innermost lamella.

Certain corpuscles which are found in the bill of some water-birds, exhibit so obviously a transition between the simple corpuscles of Herbst and the complex corpuscles of Pacini immediately to be described, that they may be especially mentioned here. These, which are sometimes named after the anatomists who first described them, the *corpuscles of Key and Retzius* (fig. 401), differ from the corpuscles of Herbst in having a capsule, composed of a large number of closely-arranged lamellæ, similar to those of the inner or denser part of the



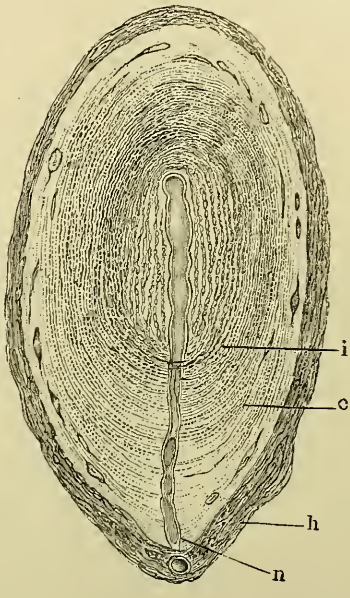


Fig. 400.—Middle part of a Herbst corpuscle of the sparrow. Osmic preparation. (W. Krause.) $\frac{500}{1}$.

h, outer longitudinal fibrous layer; *r*, felt work of transverse fibres; *i*, core, with two rows of nuclei; *t*, axis-cylinder.

Fig. 401.—Key-Retzius corpuscle in optical longitudinal section. Bichromate preparation. (W. Krause.) $\frac{400}{1}$.

h, outer layer; *c*, *i*, concentric lamellæ of capsule; *n*, terminal nerve-fibre.

Pacinian corpuscle, outside which is a single strong layer of longitudinally disposed fibrous tissue. The inner lamellæ are largely composed of circular or transverse fibres, but these lack the brownish tint of the fibres of the inner lamella of the Herbst corpuscle, nor do they exhibit the intra-lamellar fluid which is characteristic of most of the lamellæ of the Pacinian corpuscle.

Corpuscles of Vater or Pacinian bodies.—In dissecting the nerves of the hand and foot, certain small oval bodies like little seeds, are found attached to their branches as they pass through the subcutaneous fat on their way to the skin; and it has been ascertained that each of these bodies receives a nervous fibre which terminates within it. The objects referred to were described and figured by Vater (1741), as attached to the digital nerves, but he did not examine into their structure, and his account of them seems not to have attracted much notice. In more recent times, their existence was again pointed out by Cruveilhier and other French anatomists, as well as by Pacini of Pisa, who appears to be the first writer that gave an account of the internal structure of these curious bodies, and clearly demonstrated their essential connection with nerve-fibres. The researches of Pacini were followed up by Henle and Kölliker, who named the corpuscles after him; and the Pacinian corpuscles have since been the subject of numerous papers, to which the

reader is referred for details regarding their distribution and variations, that cannot be conveniently introduced here.[1]

The little bodies in question are, as already said, attached in numbers to the branches of the nerves of the hand and foot (fig. 402), and here and there one or two are found on other cutaneous nerves. They have been discovered also within the abdomen on the nerves of the solar plexus, and they are nowhere more distinctly

Fig. 402.—A nerve of the middle finger, with Pacinian bodies attached. Natural size. (After Henle and Kölliker.)

seen or more conveniently obtained for examination, than in the mesentery of the cat, between the layers of which they exist abundantly. They have been found on the pudic nerves in the penis and clitoris, bulb of the urethra, and other parts, on the intercostal nerves, sacral plexus, cutaneous nerves of the upper arm and neck, nerves of the nipple and mammary gland, and on the infra-orbital nerve. Lastly they have been recognised on nerves to tendons and ligaments, and more rarely on intra-muscular nerves, on the periosteal nerves, and, in considerable numbers, on the nerves of the joints. In many mammals they occur in masses of from 20 to 80 corpuscles imbedded in the fat of the ball of the foot and also in the interosseous space between the radius and ulna, and between the tibia and fibula. They are found in individuals of all ages. The figure of these corpuscles is oval, somewhat like that of a grain of wheat,—regularly oval in the cat, but mostly curved or reniform in man, and sometimes a good deal distorted. Their mean size in the adult is from $\frac{1}{15}$th to $\frac{1}{10}$th of an inch long, and from $\frac{1}{25}$th to $\frac{1}{20}$th of an inch broad. They have a whitish, opaline aspect : in the cat's mesentery they are usually more transparent, and then a white line may be distinguished in the centre. A slender stalk or peduncle attaches the corpuscle to the branch of nerve with which it is connected. The peduncle contains a single medullated nerve-fibre ensheathed in perineurium, with connective tissue and one or more fine blood-vessels ; it joins the corpuscle at or near one end, and conducts the nerve-fibre into it. The little body itself, examined under the microscope, is found to have a distinct lamellar structure (fig. 403). It consists, in fact, of numerous concentric membranous tunics encasing each other like the coats of an onion. Surrounded by these tunics, and occupying a cylindrical space in the middle of the corpuscle, is the core, formed of transparent and seemingly homogeneous soft substance, in the midst of which the prolongation of the nerve-fibre is contained. The number of tunics is various ; from forty to sixty may be counted in large corpuscles. Those which are situated next to the central or median cavity, and comprehending about half of the entire number, are thinner and closer together than the more exterior ones, seeming to form a system by themselves, which gives rise to a white streak often distinguishable along the middle of the corpuscles when seen on a dark ground. Outside of all, the corpuscle has a coating of ordinary connective tissue.

The lamellæ or tunics correspond very closely in structure to the lamellæ of the

[1] A complete list of papers which had appeared up to 1880 on this subject (and, indeed, not only on the Pacinian corpuscles, but on all the several kinds of terminal corpuscles and other sensory nerve-endings) will be found in a monograph by Prof. Fr. Merkel, "Ueber die Endigungen der sensiblen Nerven in der Haut der Wirbelthiere." Rostock, 1880. A concise *resumé* and classification of the sensory end-organs, by Prof. W. Krause, will be found in the "Biologisches Centralblatt," May and June, 1884.

perineurium of a nerve. Each lamella (fig. 404) consists of a connective tissue layer formed both of white fibres, which have mostly a transverse direction and are placed near its surfaces (*b*), and of elastic fibres, which pass in various directions, and (with occasional bands of white fibres) stretch across the thickness of the lamella from one surface to the other (*c*). The surfaces of the lamellæ are covered

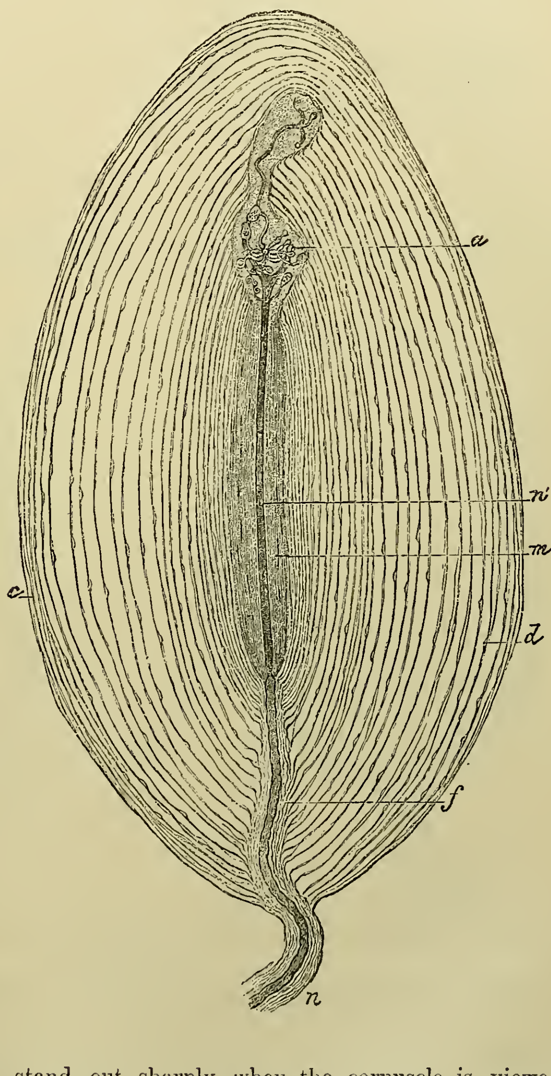


Fig. 403. — Magnified view of a Pacinian body from the cat's mesentery. (Ranvier.)

n, stalk with nerve-fibre enclosed in sheath of Henle passing to the corpuscle ; *n'*, its continuation through the core, *m*, as a pale fibre ; *a*, termination of the nerve in the distal end of the core. In the corpuscle here figured the termination is arborescent. *d*, lines separating the tunics of the corpuscle, often taken for the tunics themselves ; *f*, channel through the tunics, traversed by the nerve-fibre ; *c*, external tunics of the corpuscle.

with a layer of endothelial cells (*a*), which can be brought to view with nitrate of silver, and then their continuity with the similar cells in the perineurium is made manifest (fig. 405). The tissue of each lamella is lax as compared with that of the layers of the perineurium, and the interstices between the fibres are occupied by a considerable quantity of watery fluid, probably of the nature of lymph, and containing occasionally lymph - corpuscles. This fluid in the fresh state tends to obscure the delicate fibres of the lamellæ, so that the adjacent layers of endothelial cells belonging to the successive lamellæ stand out sharply when the corpuscle is viewed in optical section, and were long taken to represent the actual tunics of the organ. The layers are not however everywhere in such close juxtaposition, but are here and there separated from one another by interlamellar spaces which are occupied by lymph, and represent the lymphatic clefts between the layers of the perineurium of a nerve.

The nerve-fibre, the disposition of which may now be noticed, is conducted along the centre of the stalk, enters the corpuscle, and passes straight into the core, at the further end of which it terminates. As shown by Pacini, the layers of the

perineurium successively become continuous with, or rather expand into the tunics of the corpuscle. Since, however, in most Pacinian corpuscles there are many more tunics in the corpuscle than layers of the perineural sheath which invests

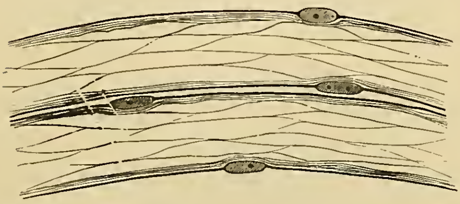
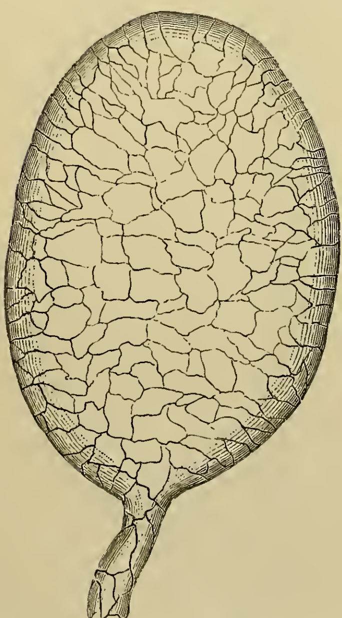


Fig. 404.—Diagrammatic representation of two tunics of a Pacinian corpuscle in transverse section.

a, *a*, epithelioid layers; *b*, *b*, connective tissue layer, more condensed near the surface; *c*, open network of fine elastic fibres in the substance of the lamella.

the entering nerve, it is only a few of the tunics which are thus continuous; and it will be generally found that it is the outer ones which are so. A certain number of the inner tunics are superadded therefore, and when traced towards the nerve-fibres they may be seen to end with rounded margins bounding a canal in which the nerve-fibre



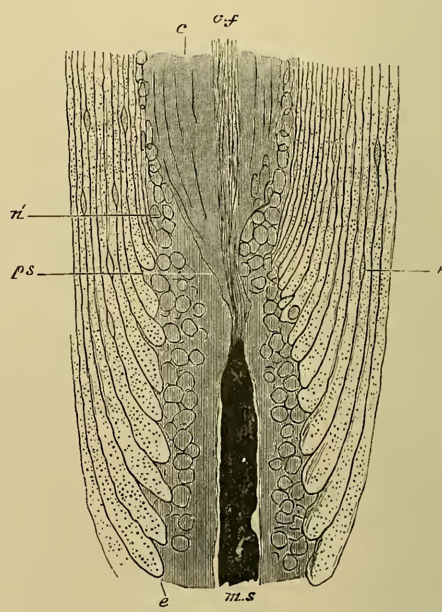


Fig. 405.—Pacinian corpuscle from the mesentery of the cat; stained with nitrate of silver. Magnified.

The epithelioid cells of the outermost tunic are shown, and their continuity, at the peduncle, with those of the corresponding layer of the perineurium (from a drawing by G. C. Henderson).

Fig. 406.—Part of Pacinian body showing the nerve-fibre entering the core. From an osmic acid preparation. (E. A. S.)

ms, entering nerve-fibre, the medullary sheath of which is stained darkly, and ends abruptly at the core; *p*, *s*, prolongation of primitive sheath, passing towards the outer part of the core; *c f*, axis-cylinder passing through the core as the central fibre; *e*, some of the inner tunics of the corpuscle, enlarged where they abut against the canal through which the nerve-fibre passes; *n*, nuclei of the tunics; *n'*, nuclei of the endoneurium, continued by others in the outer part of the core.

runs. The latter is accompanied by a little endoneural connective tissue which generally contains a number of granular cells (fig. 406).

The nerve-fibre is single as it runs along the peduncle, unless when the latter supports two corpuscles ; it retains the medullary sheath until it reaches the core, into which the axis-cylinder alone passes, freed from its primitive and medullary sheaths. In its course through the core it is somewhat flattened, and presents the appearance either of a pale, finely striated, and very faintly outlined band or stripe, or of a darker and more sharply defined narrow line ; differing thus in appearance according as its flat side or its edge is turned towards the eye. The contrast in the appearance of the fibre before and after entering the core is well exhibited after treatment with osmic acid, which stains the medullary sheath deeply, whereas the axis-cylinder is far less stained. It sometimes happens that the fibre regains its double contour for a short space, and changes again before it terminates ; this is especially liable to occur while it passes through a sharp flexure in a crooked core. The fibre usually ends by a sort of knob at the further extremity of the core, which is here itself somewhat dilated. The knob, often finely granular, appears to be an expansion of the axis-cylinder, and is sometimes of considerable size. It may be of an irregular shape with processes branching outwards from the sides, and in such cases has been taken to represent a nerve-cell ; but the characteristic nucleus of the latter is absent. The ultimate destination of the processes is unknown. The axis-cylinder shows the usual longitudinal fibrillation as it passes through the core, and the fibrils become somewhat spread out as they pass into the terminal expansion. In many cases the fibre, either immediately before terminating, or in its course through the core, divides into branches. In case of division of the fibre, the core is generally, but not invariably, divided in a corresponding measure, and the inner tunics present a figure in keeping with it. It is worthy of remark, that the nerve-fibre in its course along the core runs almost exactly in the axis of the latter, and it maintains this position even when passing through the abrupt flexures of an irregularly shaped core. It sometimes happens that a fibre passes quite through one corpuscle and terminates in a second, resuming its original size and dark outline while passing from the one to the other. A little artery enters the Pacinian body along with the nerve, and soon divides into capillary branches, which run up between the tunics. They then form loops, and return by a similar route into a vein corresponding to the artery : a single capillary usually accompanies the nerve as far as the core, and passes some way on the wall of the latter, sometimes with a spiral direction (Bowman). Occasionally a vessel enters the corpuscle at the distal end and passes towards the core, uniting the tunics in its passage.

As to the nature of the core of the Pacinian body, there is considerable difference of opinion. That it is not merely an expansion of the medullary sheath of the nerve-fibre, as was thought by Engelmann, is shown by its behaviour with staining fluids, and particularly osmic acid (see fig. 406). Moreover in cases where the medullary sheath is prolonged for some distance to the core, as occasionally happens, the contrast between it and the substance which surrounds it, is very marked.

In considering the true nature of the core, it should first be remarked that it is not completely homogeneous and structureless, as on superficial examination it seems to be, but exhibits at least in its outer part longitudinal striation and nuclei in variable number. In transverse section the striation in the outer part of the core is seen to be concentric, and produced apparently by flattened nucleated cells, which are so arranged as to inclose the inner and more homogeneous portion. At the entrance of the nerve-fibre into the core the nucleated cells here spoken of are to all appearance continuous with a layer of cells in the endoneurium around the entering nerve-fibre, so that this outer part of the core, at least, might be regarded as formed by an expansion of endoneurium. The inner part, on the other hand, that, namely, which is in immediate contact with the axis-cylinder, appears structureless. In its behaviour towards staining re-agents, it resembles protoplasm, and it is possible that it may represent the protoplasmic layer which in young nerves intervenes between the axis-cylinder and the sheath of Schwann of a nerve-fibre, and in which the fatty substance of the medullary sheath becomes deposited.

Nothing positive is known concerning the special purpose in the animal economy which

these terminations of the nerves are destined to fulfil. It is very probable, however, that the series of concentric endothelial membranes with interposed fluid is an arrangement for converting the effect of mechanical traction into fluid pressure upon the nerve, so that tension and traction of the tissue in which the corpuscle is placed, may affect the axis-cylinder in the same manner as ordinary pressure.

Little also is known as to their development, except that when first visible they appear in the form of small agglomerations of cells amongst which the termination of a nerve-fibre becomes lost to view.

Other modes of ending of sensory nerves.—Instead of ending in the special terminal corpuscles of different kinds which have been described in the preceding pages, many sensory nerves, as before stated, terminate in the form of fine ramifica-

Fig. 407.—Distribution of nerves in a portion of the cornea of the rabbit. (Ranvier.)

The nerves are stained with chloride of gold. *p*, larger plexus of non-medullated fibres, made up of numerous fine fibrils ; *a*, *a*, smaller fibres derived from them, and themselves giving off still smaller branches ; *h*, varicose fibrils ; *t*, junctional branches of the larger plexus.

tions of the axis-cylinder, which pass between the elements of the tissue to which the nerves are distributed, and may either simply come in contact with them, or, it is believed, may in some cases form an actual connection with the cells. As they approach their termination the sensory nerve-fibres, which are generally medullated, divide dichotomously again and again, retaining after all the earlier divisions both the medullary sheath and the primitive sheath, and being accompanied by a prolongation of the sheath of Henle. Lower down this last-named sheath becomes lost, and a short distance further on the medullary sheath also disappears, the nerves being continued as pale fibres enclosed only by the nucleated sheath of Schwann. Within this it can distinctly be seen in preparations stained with chloride of gold, that the axis-cylinder is made up of fine varicose fibrils (fig. 407). At every division of the nerve some of these fibrils pass into each branch, and where, as often happens, the branches unite with one another so as to form a subterminal plexus, some of the fibrils pass across from one branch to another. By the time the terminal ramification is reached many of the branches may consist of only one or two ultimate fibrils (*h*). It is generally found that the sheath of Schwann has ceased long before this condition is arrived at, although nuclei apparently like those of that sheath may often be still seen here and there upon the branches, especially at the points of bifurcation. Finally the branches of the nerve, thus reduced to the condition of ultimate fibrils, often varicose, pass between the tissue elements, and may there form an actual network by joining one

with another and becoming fused together at the points of junction, or may end either simply or with small knobbed extremities without uniting with other fibrils into a nervous network ; or, according to the view of some histologists, may pass into the cells of the tissue and thus terminate.

A "nervous network" is not to be confounded with a "nervous plexus." In the former an actual fusion of the ultimate fibrillæ which result from the division of the axis-cylinders of the nerves is assumed to take place, whereas in the latter, although there may appear to be an intimate union between the different nerves which enter into the plexus, this union does not extend to the ultimate elements of the nerve-fibre : in other words, although fibres or parts of fibres (fibrils) may be given and received by the several nerves to and from one another, these fibres (in the case of the larger plexuses) or fibrils (in the microscopic plexuses) remain completely distinct, although they may run in close juxtaposition. Nervous plexuses are of very common occurrence, both those of the larger sort which have long been recognized by anatomists, and the smaller microscopic plexuses which are very often found near the endings, both of some centripetally conducting, and of some centrifugally conducting nerves. But nervous networks are far less frequent than has been supposed, although they were until lately described as a mode of nerve-termination not by any means rare, and indeed their existence is now doubted altogether by some histologists. (Compare *Waldeyer*, Ue. d. Endigungsweise der sensiblen Nerven : Archiv. f. mikr. Anat. XVII. s. 367.)

Nerve-endings in tendons.—Special modifications of the plexiform mode of ending of sensory nerves have been described in various peripheral organs, but those

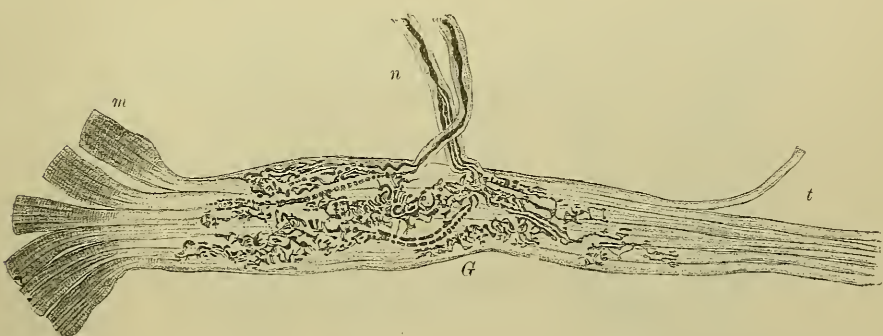


Fig. 408.—Organ of Golgi from the human tendo achillis. Chloride of gold preparation. (Ciaccio.)

m, muscular fibres ; *t*, tendon-bundles ; *G*, Golgi's organ with the axis-cylinder of the nerves, *n*, ramifying between the small connective tissue bundles.

only which are found in the tendons of muscles will here be noticed, the modes of termination in other parts being deferred until the several organs are treated of.

Most of the nerve-endings in tendon seem referable to one or other of the end-organs which have already been described, although they present considerable modification of form. In some tendons end-bulbs like those in the conjunctiva are found (Sachs), and small Pacinian corpuscles of simple structure occur occasionally in the areolar tissue sheaths of tendons and ligaments. But in many tendons, at their junction with the muscles, there occur, as was first shown by Golgi, long spindle-shaped bodies, composed apparently of a number of tendinous bundles more or less fused into one, into which one or more medullated fibres pass, and after dividing a certain number of times, their axis-cylinders spread themselves out between the smaller tendon bundles, and collectively form a branched expansion which is not unlike the terminal ramification in which the motor nerves to the muscles themselves end (fig. 408). The peculiar spindle-shaped organ, which is thus provided with a rich nervous network, is known as an *organ of Golgi*. Various

modifications of these have been described but their fundamental structure appears to be the same in all vertebrates.

In muscles themselves little or nothing is known as to the endings of sensory nerves, although that they possess such is shown by the pain which is felt when a muscle is cut. Kerschner has described the "muscle spindles" (see p. 301) as representing such sensory nerve-endings, but this view has not been generally accepted.

TERMINATION OF MOTOR NERVES.

In the **involuntary muscles** such as those which constitute the muscular layers of the hollow viscera, the nerves, which are for the most part non-medullated with a small intermixture of white fibres, form complicated plexuses as they near their termination. At the junctions of the fine nervous cords which compose the plexuses groups of ganglion-cells are in many parts met with; a well known example

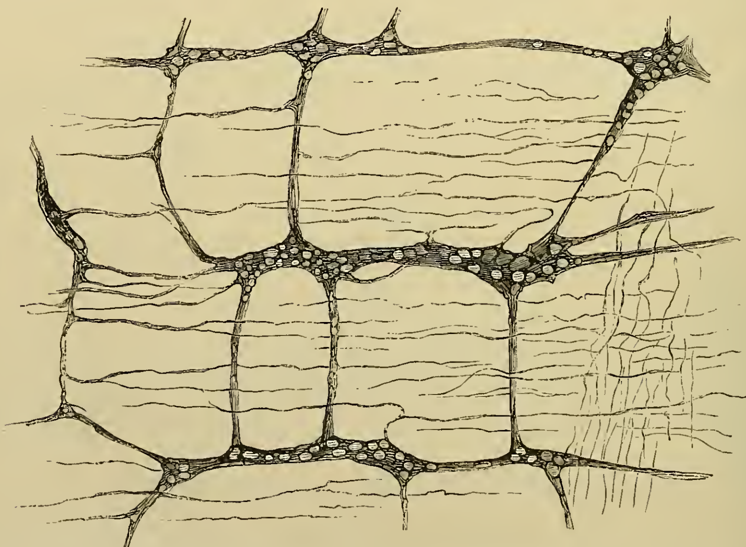


Fig. 409.—Nervous plexus of Auerbach from the muscular coat of the intestine. (Cadiat.)

of such a gangliated plexus being the *plexus myentericus* of Auerbach between the longitudinal and circular layers of the muscular coat of the intestine (fig. 409). From these gangliated plexuses branches are sent off, which penetrate between the elements of the involuntary muscular tissue, coursing for the most part parallel with the muscular fibres. The pale nerve-fibres bifurcate and give off branches at acute angles at frequent intervals, and eventually become separated into fine filaments which may represent ultimate fibrillæ, but the branches which are given off only rarely, according to Löwit, become united with those from adjoining nerve-fibres, so that it can scarcely be said that an intramuscular plexus, and still less a network, really exists. The fine longitudinally coursing fibrils come into close relation with the involuntary muscle-cells, but do not appear to pass into the interior of the cells and their nuclei. They are said to end by gradually tapering or varicose extremities, but according to Elischer each nerve-fibril terminates by a slight bulbous expansion opposite the nucleus of a contractile cell.

In the **cardiac muscular tissue** the nerves form networks with very long meshes. The nervous fibrils become closely applied to the muscular fibres, often

appearing to end in small bulbous extremities, but, according to Fischer, do not penetrate the muscular fibres. Motorial end-plates, such as occur in voluntary cross-striated muscle, are not found in the heart.

The **nerves of voluntary muscles** terminate for the most part in special expansions, to which the term *motorial end-plates* has been applied. The term *end-organ* is however a more suitable one, for, as will immediately be explained, the termination of the nerve is rather of the nature of a flattened ramification than a continuous plate.

As was mentioned in the account of the muscular tissue, the nerves in the voluntary muscles form plexuses, of which the branches grow finer and the meshes closer as they advance further into the tissue. The individual fibres, while still associated in small bundles, undergo division (fig. 388), and at length single dark-bordered fibres pass off to the muscular fibres. These nerve-fibres on approaching or reaching a muscular fibre often divide still further. The branches retain their medullary sheath until they reach the sarcolemma, when the white substance abruptly terminates, while the neurolemma becomes continuous with the sarcolemma (fig. 410, *s*). It would seem that the prolongation of the nucleated sheath of Henle is also continued over the end-organ, which thus receives a double covering

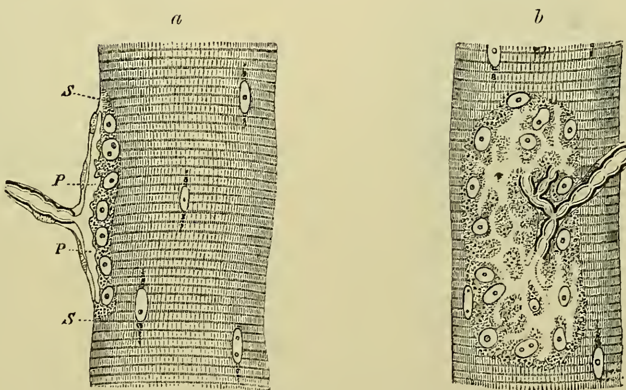
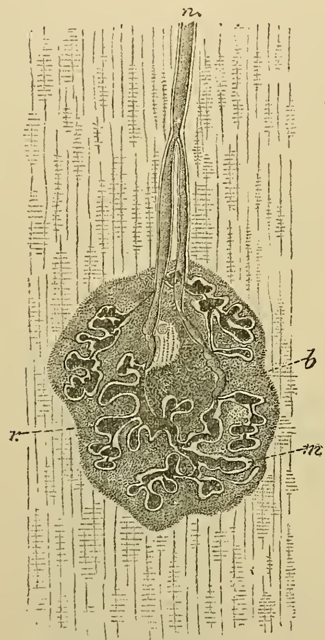


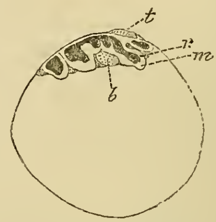
Fig. 410.—Nerve-ending in muscular fibre of a lizard (Lacerta viridis) (Kühne.) (Highly magnified.)

a, end-organ seen edgeways; *b*, from the surface. *s*, *s*, sarcolemma (here sometimes termed "telolemma"); *p*, *p*, expansion of axis-cylinder. Beneath this is granular protoplasm containing a number of large clear nuclei and constituting the "bed" or "sole" of the end organ. In *b* the expansion of the axis-cylinder appears as a clear network, branching from the divisions of the medullated fibre.

to which the name *telolemma* has been given by Kühne. The axis-cylinder as it passes into the fibre forms a clear localised branched expansion (*p p*), which lies immediately under the sarcolemma, embedded in a layer of granular matter, the "bed" or "sole" of the end-organ, which contains a number of large clear nuclei, each having one or more distinct nucleoli. The termination of the axis-cylinder is not a continuous plate, as was thought by Rouget, but appears when viewed from the surface in the form of an arborescent figure (figs. 410 to 415), the branches of which do not, according to Ranvier, anastomose. According to Kühne the branching figure which is formed by the axis-cylinder is composed of an axial part, staining darkly with gold, and a peripheral part or stroma, which remains unstained. Kühne regards the axial part as representing the fibrils of the axis-cylinder, but it may be doubted whether the differentiation into axial part and stroma is not due to the shrinking of the axis-cylinder under the influence of the reagent. The appearance of the two

parts in gold preparations is well exhibited in figs. 411, 412. Applied to the branches of the ramification small granular nuclei (fig. 414, *n*) are seen at intervals; these nuclei of the arborisation are different from the clear nuclei of the bed (*n'*), and also from the flattened nuclei of the sheath which lie immediately under the sarcolemma covering the end-plate, and which resemble the nuclei of the sheath of Schwann of the nerve. The sarcolemma over the situation of the nerve-ending is slightly raised above the general surface (fig. 410, *a*). It would appear that in mammals each





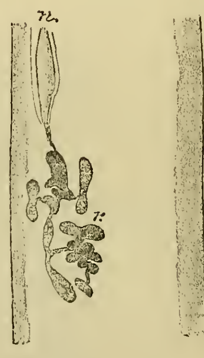


Fig. 411.—Motor end-organ of a lizard: gold preparation. (Kühne.)
n, nerve-fibre; *r*, terminal ramification of axis-cylinder; *m*, clear substance surrounding the ramification (matrix); *b*, granular bed or sole of the end-organ.

Fig. 412.—Cross-section of muscular fibre and end-organ of lizard: gold preparation. (Kühne.)
r, terminal ramification of axis-cylinder; *m*, matrix; *b*, nucleus of bed; *t*, nucleus of telolemma.

Fig. 413.—Motor end-organ of human muscle: gold preparation. (Kühne.)
n, medullated nerve-fibre; *r*, terminal ramification of axis-cylinder.

muscular fibre has but one terminal structure, and receives consequently but one nerve-fibre. As, moreover, the fibres of a nerve undergo division, probably repeated division, before ending, it follows that one fibre in a nerve-root or -trunk may supply several muscular fibres. In reptiles the longer muscular fibres may have two or more nerve-endings.

The shape and extent of the terminal ramification of the axis-cylinder within the end-organ varies greatly, not only in different classes of animals, but also in animals belonging to the same class, and there is even some variation in individuals of the same species, as is evident from the various representations of the end-organs of the green lizard, which are here given. On the whole, it may be stated that the terminal ramification is most compact in mammals and reptiles and least so in

amphibia (fig. 415), where there is no continuous granular bed with clear nuclei imbedded in it, and the ramifications of the axis-cylinder are extended over a much larger proportionate area of the fibre than in reptiles, birds, and mammals, so that the termination of the nerve is far less localised. The branches of the axis-

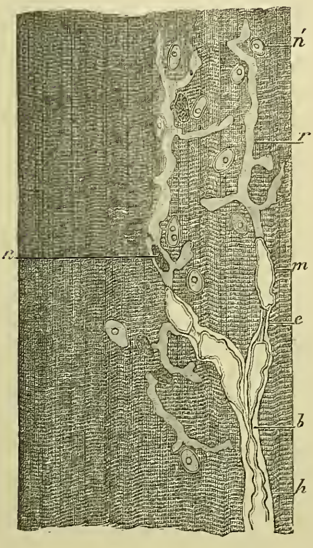


Fig. 414.—Termination of a nerve in a muscular fibre of the lizard (Lacerta viridis). (Ranvier.) Highly magnified.

h, sheath of the nerve-fibre; *b*, bifurcation of the fibre; *e*, node; *m*, short segment beyond the node; *r*, terminal ramifications of the axis-cylinder; *n*, nuclei on the branches of the axis-cylinder; *n′*, nuclei in the granular substance of the end-plate. The granular substance lies in the intervals between the branches of the axis-cylinder; it is not seen in this figure.

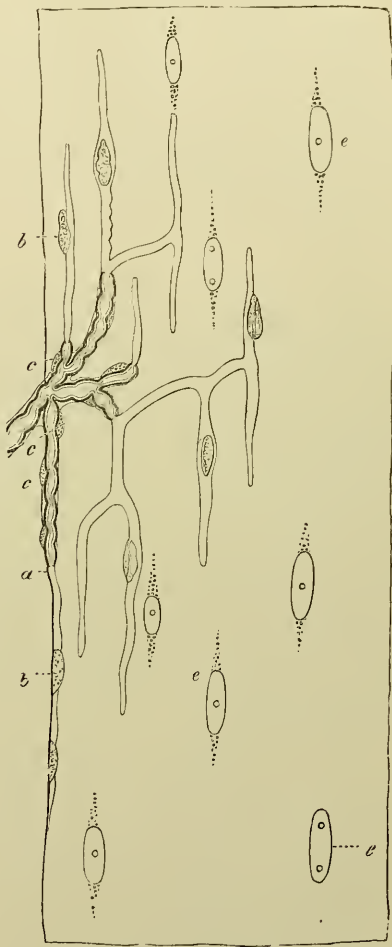


Fig. 415.—Nerve-ending in muscle of frog. (Kühne.)

a, one of the branches of the medullated fibre passing within the sarcolemma; *b*, *b*, granular pear-shaped nuclei of the arborisation; *c*, *c*, nuclei of sheath; *e*, *e*, muscle-nuclei.

cylinder run for a short distance parallel with the axis of the fibre between the sarcolemma and muscular substance, terminating abruptly by rounded extremities. They have here and there slight enlargements, connected with which are seen, as in the end-plate of the lizard, granular pear-shaped nuclei (*b*), entirely different in appearance from the proper nuclei of the muscle (*e*). In other animals, *e.g.*, in snakes, there is a tendency for the branches of the ramification to become dilated at their termination into bulbous enlargements, which in a well-stained preparation gives an appearance like that of a bunch of berries. Many other variations are met with, but in no case is there a departure from the general rule that the ultimate

termination is in the form of a ramification of the axis-cylinder on the surface of the fibre within the sarcolemma.[1]

The termination of motor nerves in special granular expansions within the sarcolemma was first noticed by Doyère in insect-muscles. The aborescent termination of the axis-cylinder was discovered in the frog by Kühne in 1862. In the same year the end-plates were recognised by Rouget in the lizard, and in 1863 by W. Krause in mammals. The last named observer was the first to describe the termination of the axis-cylinder as a ramified expansion imbedded in granular substance, but maintained that the whole structure lay outside the sarcolemma. In this opinion Krause is supported by Kölliker, but by far the majority of observers regard the whole end-organ as hypolemmal in position. Engelmann and Fœttinger have been led from observations upon insect-muscles to the conclusion that the expansion of the nerve-fibre comes into actual continuity with the isotropous substance, *i.e.*, with the sarcoplasm, of the muscular fibre. But the effect of section of a motor nerve in the living animal—the resulting degeneration extending no further into the muscular fibre than the end-plate itself—is a strong argument against the existence of any such anatomical continuity.

DEVELOPMENT OF THE NERVES.

The embryonic development of the nerves has already been treated of in the part of this work devoted to Embryology. It was there shown that all nerve-fibres and nerve-cells, whether belonging to the central nervous system or to the peripheral and sympathetic nerves, are originally derived from the neural or neuro-sensory epiblast, and that in the case of the afferent nerve-fibres, such as those of the posterior roots, the axis-cylinders grow from the cells of origin (neuroblasts of the spinal ganglia), both centripetally into the nerve-centre, and centrifugally towards the peripheral sensory parts, while in the case of the efferent nerve-fibres, those namely of the anterior roots, the axis-cylinders grow only centrifugally from their cells of origin, which here lie within the nerve-centre (neuroblasts of the nerve-centres), and thence eventually pass to and unite with the muscular fibres. So far as is known, this is the only mode of development of nerve-fibres, viz., as out-growths from nerve-cells or neuroblasts, and they always, whether in the nerve-centres or in the nerve-trunks, at first appear as pale fibres, destitute both of primitive and of medullated sheath.

It appears somewhat doubtful whether the pale fibres which are thus first formed are single axis-cylinders or bundles of such. However this may be, they early become surrounded by cells from the adjacent mesoblast, which penetrate also between them, and eventually produce the connective tissue of the nerve-sheath (epineurium, perineurium, endoneurium). In the nerve-centres very little connective tissue passes between the nerve-fibres, which are there supported by the spongioblasts (see Embryology, p. 58). These are cells which have a common (epiblastic) origin with the neuroblasts, although their function, according to His, is early differentiated.[2] From the spongioblasts, neuroglia cells appear ultimately to be produced, and these, within the central nervous system, take on much the same supporting function which is elsewhere fulfilled mainly by connective tissue.

The medullary sheath does not make its appearance until a comparatively late period of embryonic life, and there is much doubt as to its mode of formation. It first appears as a thin layer of myelin, not unfrequently interrupted, which closely ensheaths the axis-cylinder, and is itself ensheathed by the nucleated neurolemma or sheath of Schwann which has been previously formed. Vignal refers the formation

[1] For an account of the variations which are met with in different animals, illustrated by a large number of drawings, and for a discussion of many disputed points regarding the details of structure of these organs, the reader is referred to a paper by Prof. W. Kühne in the "Zeitschrift f. Biologie," Bd. 23, 1886.

[2] Ramón y Cajal, however, states that many of the neuroblasts are directly derived from cells which are identical with the spongioblasts of His.

of the medullary sheath to the cells which compose the nucleated sheath of Schwann, and the same view has been taken by other observers; but it must nevertheless be regarded as possible that it is actually formed by the axis-cylinder, or by the protoplasm which forms the peripheral layer of the axis-cylinder in its embryonic condition, and for the following reasons, viz. (1) that in the central nervous system the medullated nerve-fibres never at any time possess this nucleated sheath ; (2) that in regenerating nerve-fibres, a thin medullary sheath appears around the growing axis-cylinders before these are surrounded by their special nucleated sheath. At the same time it is possible to suppose that the cells of Schwann's sheath may influence the deposition of myelin. The neurolemma or sheath of Schwann on the other hand appears certainly to be formed by cells which have applied themselves to and have become flattened out around the preformed axis-cylinder, but whether they are to be regarded as of mesoblastic origin (Vignal, Kölliker), or whether they have passed out from the nerve-centre along with the processes of the neuroblasts, and are therefore like the latter epiblastic in nature, is a question which requires further investigation. On the whole, although we have no certain information on the subject, it is probable that the medullary sheath has an origin in common with the axis-cylinder, but that the primitive sheath is different, and not improbably mesoblastic in origin.

The formation of the medullary sheath occurs, not simultaneously over the whole nervous system, but in regular order along definite tracts, and the knowledge of this in the hands of Flechsig, has proved an important means of tracing the course of certain strands of fibres in the nervous centres, as will be noticed when the subject of the continuity of the fibres in those centres is dealt with.

The fact that the nerve-segments or internodes of the peripheral nerves are considerably shorter in the young animal, points to the existence of an interstitial as well as a terminal growth of nerve-fibres. Besides such expansion of the internodes, Vignal has described another method of growth in length of nerve-fibres ; mesoblast cells similar to those which originally produced the nucleated sheath, applying themselves to the axis-cylinder of the nodes, and determining first an increase in length of the nodal axis-cylinder, and then a formation of myelin upon this, so that a short segment becomes intercalated at the node. These short segments soon grow so as to attain the length of the remaining segments of the nerve-fibre.

Degeneration and regeneration of nerves.—The divided ends of a nerve that has been cut across readily reunite by cicatricial tissue, but the cut ends of the fibres themselves do not thus unite. On the contrary, soon after the section, a process of degeneration begins in the peripheral or severed portion of the nerve. The nuclei become multiplied, and the protoplasm about them largely increased in amount, the segments taking on to some extent their embryonic condition. At the same time the medulla of the white fibres degenerates into a granular mass consisting of fatty molecules, and is then totally removed, and eventually the axial fibre also disappears (fig. 416, A, B, and C).

In regeneration the new fibres grow afresh from the axial fibres of the central end of the divided nerve-trunk (often more than one from each) ; and, penetrating into the peripheral end of the trunk, grow along this as the axis-cylinders of the new nerves, becoming after a time surrounded with medullary substance (fig. 416, D).

To this brief summary the following details may be added :—In warm-blooded animals the first changes in the peripheral part of the nerve are seen twenty-four hours after the section. The nuclei underneath the primitive sheath are everywhere found hypertrophied, the primitive sheath is distinctly visible, and protoplasm is found to have accumulated at the expense of the medullary sheath, both in the immediate neighbourhood of the nuclei, at the nodes, and also at other points in

the fibre, which correspond, according to Ranvier, with the intervals between the medullary segments. Fifty hours after the section in the rabbit (but not till four days in the dog) the protoplasmic aggregations are found here and there altogether to interrupt the continuity of the medullary sheath, and they contain numerous fatty granules, and sometimes droplets of myelin (fig. 416, A). About the fourth day the nuclei are seen to be multiplied, but not to any great extent (C); and

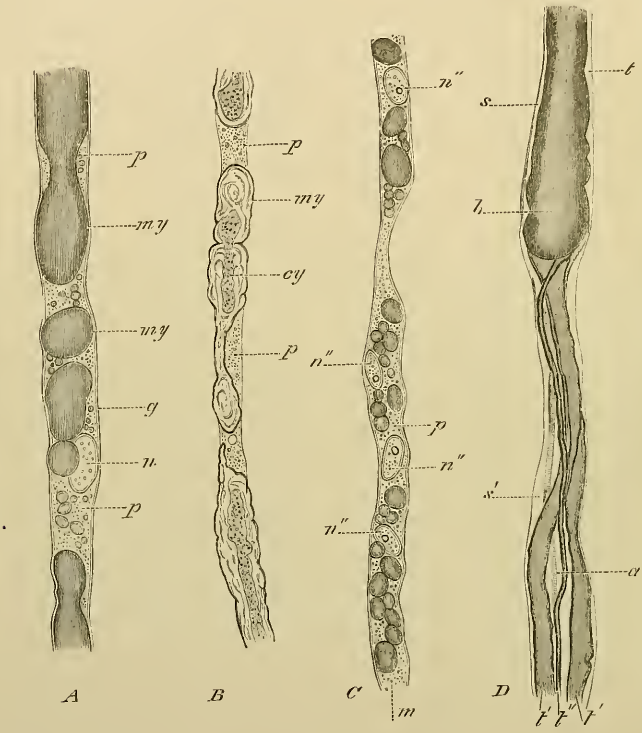


Fig. 416.—Degeneration and regeneration of nerve-fibres in the rabbit. (Ranvier.)

A, part of a nerve-fibre in which degeneration is commencing in consequence of section (50 hours previously) of the trunk of the nerve higher up; *my*, medullary sheath becoming broken up into drops of myelin; *p*, granular protoplasmic substance which is replacing the myelin; *n*, nucleus, not yet multiplied; *g*, primitive sheath. B, another nerve-fibre in which degeneration is proceeding, the nerve having been cut four days previously. This specimen is differently prepared from the others, so as to exhibit the axis-cylinder (*cy*) also partly broken up into portions of different length, enclosed in the myelin, *my*. C, more advanced stage of degeneration, the medullary sheath having in great measure disappeared, while several nuclei (n'', n'') have been formed by division of the single nucleus of the internode. D, commencing regeneration of a nerve-fibre. Several small nerve-fibres (t', t''), have sprouted out from the enlarged cut end (*b*) of the nerve-fibre (*t*); *a*, an axis-cylinder, which has not yet acquired a medullary sheath; *s*, s', primitive sheath.

the whole of the myelin after four or five days is broken up into drops, some larger, some smaller. The axis-cylinder is also found to be interrupted at numerous places, and remains only in the shape of short fibres, often curled round at their broken ends, enclosed in the large drops of myelin (B). Eventually these portions also may disappear. The myelin at length becomes almost entirely removed, partly through the agency of leucocytes or phagocytes, until nothing remains of it except a few isolated drops, which escape absorption, and all that then remains of the original fibre is the primitive sheath, which is occupied by a protoplasmic mass containing an increased number of nuclei. During the disappearance of the myelin

from the nerve-fibres the cells of the connective tissue in the neighbourhood of the fibres become charged with fatty granules, which may have become formed from the dissolved fatty substances of the medullary sheath.

These degenerative changes seem to occur simultaneously along the whole length of the nerve. In the nerves to voluntary muscles the end-plate is said to be the part first affected.

In the immediate neighbourhood of the section the appearances are somewhat modified by the escape of the myelin from the cut ends of the nerve-fibre, and the infiltration of blood and lymph into the interior of the ends thus emptied of their contents. This change must of course occur both in the central stump of the nerve as well as in the peripheral cut end: it does not often extend beyond the first node. Apart from such traumatic modification, true degenerative changes do not occur in the end of the nerve which is still in connection with the centre, although prolifera-tion of the nucleus in the first and second internodes near the cut may take place. The central cut end of the axis-cylinder does not become altered; except that it undergoes a slight swelling, preparatory in all probability to the renewed growth by which the regeneration of the fibre is effected.

Regeneration proceeds but slowly. Up to the twenty-eighth day after the section, or even later than this, there is still no trace of the new nerve-fibres in the peripheral part of the nerve. With the exception of a few fibres which for some reason not well understood (probably because they are derived from some other nerve which has not been cut, and are taking a recurrent course in the cut nerve), have not undergone degeneration, nothing is to be seen in a section of the nerve at this period, except the primitive sheaths of the old fibres, filled with clear or finely granular substance. If, however, a transverse section be made of a nerve considerably later than this (sixty or seventy days after the original section) it is found that within the tubes formed by the old primitive sheaths, according to Vanlair between them, small single fibres or groups of fibres, either pale or provided with a medullary sheath, are to be seen, besides here and there those drops of myelin which have remained unabsorbed from the medullary sheaths of the original fibres. On cutting out the central end of the nerve, together with the cicatrix, and separating its fibres, it is seen that the groups of small fibres noticed in the transverse section are continuous with the central ends of the axis-cylinders of the original nerve (fig. 416, D). Either a bunch of small fibres may grow directly from the axis-cylinder of one fibre, or two only may emerge from this; but these soon bifurcate, and, repeating this process again and again, may eventually form a considerable group. It would appear therefore that the regeneration of a cut nerve is effected by a growth of new fibres from the axis-cylinders of the central cut end, and that many more such fibres are formed in the first instance than the old ones which have undergone degeneration. The growth from the old axis-cylinders always occurs in the situation of a node —either the one nearest to the section or one somewhat higher up. The new fibres are at first pale but subsequently acquire a medullary sheath, still later a primitive sheath, with constrictions of Ranvier, which, as in young nerves, are placed at much more frequent intervals than in the old fibres, so that the intervals are much shorter.

The fibres which grow thus in groups from the old axis-cylinders are often very irregular in their course, twisting around one another, and even looping back in some places for a considerable distance. In the cicatrix especially is this irregularity and obliquity of disposition noticeable, probably on account of the absence here of the guide formed by the sheaths of the original fibres.

Restoration of function in the nerve may not occur for several months, during which time it may be presumed the new nerve-fibres are slowly finding their way

along the course of those which have been destroyed as a result of the section. Of the numerous fibres in the groups above described, no doubt a few only eventually assume the function of the fibres which they replace, but the later steps of the process of regeneration have not yet been fully followed out.

Except close to the actual place of section, where they are somewhat hypertrophied, the connective-tissue sheaths of the nerves remain unaltered. In the cicatrix the new nerve-fibres do not at first run in definite sheaths, but these become subsequently developed from the connective-tissue around, so that at length the restoration of continuity of all the structures in the nerve becomes complete. Vanlair states that the outbudding of the axis-cylinders of the central end may occur as much as one or two centimeters from the point of section, and may involve at first only the peripheral fibres of a funiculus.

Ranvier looks upon the regeneration of a nerve by growth from the intact central ends of the fibres as illustrating the tendency which, he believes, all nerve-fibres exhibit, to grow continuously until a hindrance is met with, and he compares the result of cutting a nerve-fibre in causing the growth of a number of new fibres in place of the original one, to that produced when the leading shoot of a plant is removed, in causing the production of a number of lateral buds.

Some have thought that under favourable circumstances an immediate union between the ends of the nerve-fibres may happen after section ; but considering the impossibility of procuring exact apposition of the individual fibres, end to end, as well as the inevitable extension of the effects of the mechanical injury caused by the section along the soft contents of the primitive sheath, it seems improbable that such direct union should ever occur.

The degeneration does not affect, as we have seen, the part of the nerve remaining in connection with the nervous centre, which seems to exert an influence in maintaining the nutrition of the nerve. The ganglia, as well as the grey matter of the brain and spinal cord, are centres of this influence. It is found that, in the central portion of a divided spinal nerve, while the fibres belonging to the anterior root owe their integrity to their connection with the spinal cord (and especially with the large cells of the anterior cornu), those of the posterior root are similarly dependent on the ganglion ; and that if the posterior root be cut between the ganglion and the spinal cord, not only will the fibres which pass from it into the trunk of the nerve beyond the ganglion remain unchanged, but also those above the ganglion, in the portion of the root left in connection with it ; whereas the fibres of the same root which remain connected with the cord but severed from the ganglion degenerate.

The degeneration of the peripheral end of a cut nerve and the breaking up of the substance of the medullary sheath were first noticed by Nasse in 1839. But the discovery by Augustus Waller in 1852 of the dependence of the process upon isolation of the nerve-fibre from its nutritive centre, and his application of this discovery to the tracing the course of nerve-fibres in peripheral parts (now known as the Wallerian method) first gave full interest and importance to the observation of Nasse. Stated briefly, the law may be formulated as follows :—" Degeneration occurs along the whole extent of any nerve-fibre which is cut off from the cell which governs its nutrition," and this, as the observations of His have shown, is in every case the cell from which the nerve-fibre has originally grown.[1]

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[1] The addendum which is sometimes made to the effect that the course of the degeneration follows that of the nervous impulses which are ordinarily conducted along the fibre is manifestly erroneous.

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BLOOD-VESSELS.

The blood, from which the solid textures immediately derive material for their nourishment, is conveyed through the body by branched tubes named blood-vessels. It is driven along these channels by the action of the heart, which is a hollow muscular organ placed in the centre of the sanguiferous system. One set of vessels, the *arteries*, conducts the blood out from the heart and distributes it to the different regions of the body, whilst other vessels, the *veins*, bring it back to the heart again. From the extreme branches of the arteries the blood gets into the commencing branches of the veins or revehent vessels, by passing through a network of fine tubes which connect the two, and which are termed, by reason of their smallness, the *capillary* (*i.e.*, hair-like) *vessels*, or, simply, the *capillaries*.

ARTERIES.

These vessels were originally supposed to contain air. This error, which had long prevailed in the schools of medicine, was refuted by Galen, who showed that the vessels called arteries, though for the most part found empty after death, really contain blood in the living body.

Mode of distribution.—The arteries usually occupy protected situations; thus, after coming out of the great visceral cavities of the body, they run along the limbs on the aspect of flexion, and not upon that of extension where they would be more exposed to accidental injury.

As they proceed in their course the arteries divide into branches, and the division may take place in different modes. An artery may at once resolve itself into two or more branches, no one of which greatly exceeds the rest in magnitude, or it may give off several branches in succession and still maintain its character as a trunk. The branches come off at different angles, most commonly so as to form an acute angle with the further part of the trunk, but sometimes a right or an obtuse angle, of which there are examples in the origin of the intercostal arteries.

An artery, after a branch has gone off from it, is smaller than before, but usually continues uniform in diameter or cylindrical until the next secession; thus it was found by Hunter that the long carotid artery of the camel does not diminish in calibre throughout its length. A branch of an artery is less than the trunk from which it springs, but the combined area or collective capacity of all the branches into which an artery divides, is greater than the calibre of the parent vessel immediately above the point of division. The increase in the joint capacity of the branches over that of the trunk is not in the same proportion in every instance of division, and there is at least one case known in which there is no enlargement, namely, the division of the aorta into the common iliac and sacral arteries; still, notwithstanding this and other possible exceptions, it must be admitted as a general rule that an enlargement of area takes place. From this it is plain that, since the area of the arterial system increases as its vessels divide, the capacity of the smallest vessels and capillaries will be greatest; and, as the same rule applies to the veins, it follows that the arterial and venous systems may be represented, as regards capacity, by two cones whose apices (truncated it is true) are at the heart, and whose bases are united in the capillary system. The effect of this must be to make the blood move more slowly as it advances along the arteries to the capillaries, like the current of a river when it flows in a wider and deeper channel, and to accelerate its speed as it returns from the capillaries to the venous trunks.

When arteries unite they are said to anastomose or inosculate. Anastomoses may occur in tolerably large arteries, as those at the base of the brain, those of the hand and foot, and the mesentery, but they are much more frequent in the smaller vessels. Such inosculations admit of a free communication between the currents of blood, and must tend to promote equability of distribution and of pressure, and to obviate the effects of local interruption.

Arteries commonly pursue a tolerably straight course, but in some parts they are tortuous. Examples of this in the human body are afforded by the arteries of the lips and of the uterus, but more striking instances may be seen in some of the lower animals, as in the well-known case of the long and tortuous spermatic arteries of the ram and the bull. In very moveable parts like the lips, this tortuosity will allow the vessel to follow their motions without undue stretching ; but in other cases its purpose is not clear. The physical effect of such a condition of the vessel on the blood flowing along it must be to reduce the velocity, by increasing the extent of surface over which the blood moves, and consequently the amount of impediment from friction ; still it does not satisfactorily appear why such an end should be provided for in the several cases in which arteries are known to follow a tortuous course. The same remark applies to the peculiar arrangement of vessels named a "rete mirabile," where an artery suddenly divides into small anastomosing branches, which in many cases unite again to re-construct and continue the trunk. Of such *retia mirabilia* there are many examples in the lower animals, but, as already remarked, the purpose which they serve is not apparent. The best known instance is that named the *rete mirabile of Galen*, which is formed by the intracranial part of the internal carotid artery of the sheep and several other quadrupeds.

Arteries possess considerable strength and a very high degree of elasticity, being extensible and retractile both in their length and their width. When cut across they present, although empty, an open orifice ; the veins, on the other hand, collapse, unless when prevented by connection with surrounding rigid parts.

Structure.—In most parts of the body the arteries are inclosed in a sheath formed of connective tissue, and their outer coat is connected to the sheath by filaments of the same tissue, but so loosely that, when the vessel is cut across, its ends

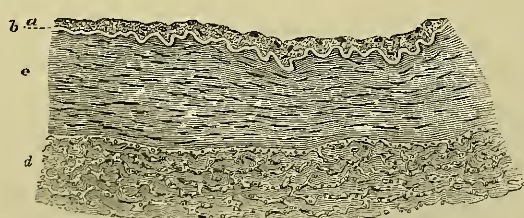


Fig. 417.—Transverse section of part of the wall of the posterior tibial artery (man). 75 diameters. (E. A. S.)

a, epithelial (endothelial) and subepithelial layers of inner coat ; *b*, elastic layer (fenestrated membrane), of inner coat, appearing as a bright line in section ; *c*, muscular layer (middle coat) ; *d*, outer coat, consisting of connective tissue bundles. In the interstices of the bundles are some connective tissue nuclei, and, especially near the muscular coat, a number of elastic fibres cut across.

readily shrink some way within the sheath. Some arteries lack sheaths, those for example which are situated within the cavity of the cranium.

Independently of this sheath, arteries (except those of minute size whose structure will be afterwards noticed) have been usually described as formed of three coats, named, from their relative position, internal, middle, and external (fig. 417, in section) ; and as this nomenclature is generally followed in medical and surgical works, and also correctly applies to the structure of arteries so far as it is discernible

by the naked eye, it seems best to adhere to it as the basis of our description; although it will be seen, as we proceed, that some of these coats are found on microscopic examination really to consist of two or more strata differing from each other in texture, and therefore reckoned as so many distinct coats by some authorities.

Internal coat (*Tunica intima*) (fig. 417, *a*, *b*). This may be raised from the inner surface of the arteries as a fine transparent colourless membrane, elastic but very easily broken, especially in the circular or transverse direction, so that it cannot be stripped off in large pieces. It is very commonly corrugated with fine and close longitudinal wrinkles, caused most probably by a contracted state of the artery after death. Such is the appearance presented by the internal coat to the naked eye, but by the aid of the microscope, it is found to consist of three different structures, namely :—

1. An *epithelial layer* (*endothelium* of the artery) (fig. 417, *a*, and fig. 418) forming the innermost part or lining. This is a simple layer of thin elliptical or irregularly polygonal cells, which are often lengthened into a lanceolate shape. The cells have round or oval nuclei, with nucleoli : their outlines are often indistinct in

Fig. 418.—Epithelial layer lining the posterior tibial artery of man. 250 diameters. (E. A. S.)

Nitrate of silver preparation.

Fig. 419.—Cell-spaces of sub-epithelial layer of artery (posterior tibial). 250 diameters. (E. A. S.)

The ground substance is stained by nitrate of silver, and the cell-spaces of the tissue are thus made manifest as white patches, the contained cells not being seen.

the fresh state, but may be brought into view by means of nitrate of silver. When the vessels are empty and collapsed, the endothelium cells are less flattened, and the part of each cell which contains the nucleus may project somewhat into the lumen of the vessel.

2. A *subepithelial layer* (striated layer of Kölliker). This is composed of a finely fibrillated connective tissue with a number of branched corpuscles lying in the cell-spaces of the tissue (fig. 419). This layer is most developed in the larger arteries : it exists however as a thin stratum in the medium-sized ones. In the aorta it is very well marked and contains a large number of anastomosing cells and cell-spaces lying in a finely fibrillated ground-substance. Longitudinal networks of

very fine elastic fibres, which are in continuity with the larger elastic fibres of the next layer, occur in it in the aorta.

3. *Elastic layer* (fig. 417, *b*). The chief substance of the inner coat is formed by elastic tissue, which occurs as longitudinal networks of fibres (fig. 420), consisting of one or more layers of different degrees of closeness. Not uncommonly some of these (or one in particular) take on a membranous character, in which case the "perforated" or "fenestrated" membrane of Henle is formed. This consists of a thin and brittle transparent film of elastic tissue. It can be stripped off in small shreds, which have a remarkable tendency to curl in at their borders, and roll themselves up as represented in fig. 421. The films of membrane are marked by fine lines, following principally a longitudinal direction, and joining each other obliquely in a sort of network. These lines are reticulating fibres formed upon the membranous layer and continuous with the reticulating elastic fibres which pervade the muscular coat on the one side and with those which extend into the subepithelial

Fig. 420.—Elastic network of artery. (Toldt.)

Fig. 421.—Portion of fenestrated membrane from the femoral artery, magnified 200 diameters. (Henle.)
a, *b*, *c*, perforations.

layer on the other. The membrane is further remarkable by being perforated with numerous round, oval, or irregularly shaped apertures of different sizes. In some parts of the arteries the perforated membrane is very thin, and therefore difficult to strip off; in other situations it is of considerable thickness, consisting of several layers; in which case it tends in the outer layers to lose its membranous character: indeed it must be borne in mind that every transition is met with between the fenestrated membranes, and the longitudinal elastic network.

The inner coat in its most developed condition may thus be said to be formed of (1) a layer of flattened epithelial cells (endothelium), (2) a layer of delicate connective tissue with branched cells; and (3) of elastic tissue under two principal forms, namely, the longitudinal elastic networks and the fenestrated membrane; and these two forms may coexist in equal amount, or one may predominate, the other diminishing or even disappearing altogether.

Middle coat (*Tunica media*) (fig. 417, *c*). This consists of plain muscular tissue, in fine bundles, disposed circularly round the vessel, and consequently tearing off in a circular direction, although the individual bundles do not form complete rings. The considerable thickness of the walls of the arteries is due chiefly to this coat; in the smaller ones, it is thicker in comparison with the calibre of the vessel. In the larger vessels it is made up of many layers; and elastic films either finely reticular, or quite similar to the fenestrated membrane of the inner coat, are found between the muscular layers and alternating with them, being also united with one

another by elastic fibres passing across the muscular bundles. In most arteries this elastic tissue of the middle coat is but slightly developed, but in the aorta (fig. 424) and carotid arteries and in some of the branches of the latter, it attains a considerable development, and since in them also elastic fibres are seen extending into the subepithelial layer of the inner coat, the distinction between the inner and middle coats as shown in section is far less marked than it is in ordinary arteries. There is also a not inconsiderable amount of connective tissue in the middle coat of the aorta.

The muscular fibre-cells of the middle coat of the arteries (fig. 422 and fig. 423) are seldom more than from $\frac{1}{300}$ to $\frac{1}{200}$ of an inch long and frequently, especially in

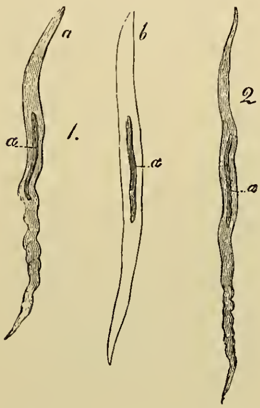


Fig. 422.—Muscular fibre-cells from human arteries. Magnified 350 diameters.

1. From the popliteal artery; *a*, natural; *b*, treated with acetic acid. 2. From a small branch of the posterior tibial (from Kölliker).

Fig. 423.—Muscular fibre-cells from superior thyroid artery (man). 340 diameters. (E. A. S.)

those arteries in which the elastic tissue of the middle coat is most developed, present a very irregular shape with jagged extremities (fig. 423). Their nuclei are distinctly rod-shaped and are often slightly curved.

Bundles of white connective-tissue fibrils may also occur in small quantity in the middle coat, the proportion increasing with the size of the artery. It is important to note that the muscular tissue of the middle coat is more pure in the smaller arteries, and that the admixture of other tissues increases in the larger-sized vessels; in these, moreover, the muscular cells are smaller. Accordingly, the contractility of the arteries, which depends on the muscular tissue of the middle coat, is little marked in those of large size, but becomes much more conspicuous in the smaller branches.

External coat (*Tunica adventitia*) (fig. 417, *d*). This is composed mainly of fine and closely-felted bundles of white connective tissue, together with a variable amount of longitudinally disposed elastic tissue between the bundles (in the figure the elastic fibres are seen cut across). The elastic tissue is much more abundant towards the inner part, next the muscular coat, and is frequently described as constituting here a distinct elastic layer: it is most marked in arteries of medium calibre, becoming thinner, and at length gradually disappearing in those of small size.

In large and middle-sized arteries the bundles of white connective tissue chiefly run diagonally or obliquely round the vessel, and their interlacement becomes much

more open and lax towards the surface of the artery, where they connect the vessel with its sheath or with other surrounding parts. Longitudinally arranged contractile fibre-cells have been described by various observers in the external coat of some arteries (*e.g.*, the iliacs, superior mesenteric, splenic, renal, dorsalis penis, and the

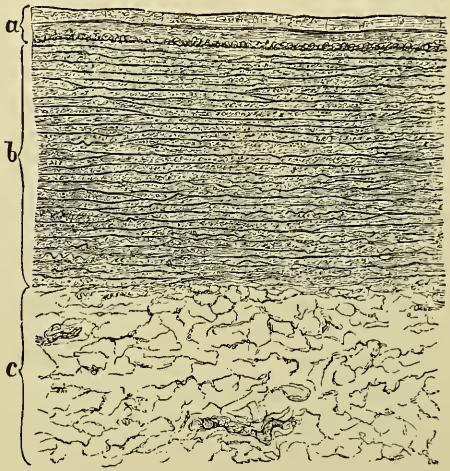


Fig. 424.—Section of thoracic aorta, as seen under a low power. (Toldt.)

a, inner coat, showing in its inner part longitudinal muscular fibres cut across ; *b*, middle coat, showing elastic membranes alternating with the muscular tissue ; *c*, outer coat, with two sections of vasa vasorum.

umbilical arteries of the fœtus). In the umbilical arteries, according to Eberth, a complete layer of longitudinal muscular fibres is also present in the middle coat, internal to the ordinary circular fibres. Scattered longitudinal muscular cells are present in some arteries amongst the circularly disposed fibres of the middle coat, and even in the subendothelial layer of the internal coat (see fig. 424, in the aorta). The outer coat is usually of greater proportionate thickness in the smaller arteries, but as it shades off into the surrounding connective tissue it is difficult to adjudge its exact thickness.

Some arteries have much thinner coats than the rest, in proportion to their calibre. This is strikingly the case with those contained within the cavity of the cranium, and in the vertebral canal ; the difference depends on the external and middle coats, which in the vessels referred to are thinner than elsewhere. The pulmonary arteries have also much thinner coats than those of the aortic system.

Vessels and nerves of arteries.—The coats of arteries receive small vessels, both arterial and venous, named *vasa vasorum*, which serve for their nutrition. The little nutrient arteries are not derived immediately from the cavity of the main vessel but pass into its coats from branches which arise from the artery (or sometimes from a neighbouring artery), at some distance from the point where they are ultimately distributed, and divide into smaller branches within the sheath, and upon the surface of the vessel, before entering the outer coat where they are distributed (fig. 424). In some of the larger mammals, a few pass into the middle coat, and follow the circular course of its fibres, but in health none penetrate into this coat in the human subject and still less into the internal coat (Ranvier). Minute venules return the blood from these nutrient arteries, which, however, they do not closely accompany, and discharge it into the vein or pair of veins which usually runs alongside the artery. Lymphatics are present in the outer coat.

Arteries are generally accompanied by larger or smaller nerves ; and when, in the operation of tying an artery, these happen to be included along with it in the ligature, pain may be experienced ; but the vessel itself, when in a healthy condition, is insensible. Nerves are, nevertheless, distributed to the coats of arteries. They form plexuses round the larger arteries, and run along the smaller branches in form of fine bundles of fibres, which here and there twist round the vessel, and unite with one another in a plexiform manner. The fine branches destined for the artery penetrate to the middle coat, to the muscular tissue of which they are chiefly distributed.

Minute ganglia are found in various parts connected with the arteries, but their existence does not appear to be by any means universal.

VEINS.

Mode of distribution.—The veins are ramified throughout the body, like the arteries, but in most regions and organs of the body they are more numerous and larger, so that the venous system is altogether more capacious than the arterial. The pulmonary veins form an exception to this rule, for they do not exceed in capacity the pulmonary arteries.

The veins are arranged in a superficial and a deep set, the former running immediately beneath the skin, and thence named subcutaneous, the latter usually accompanying the arteries, and named *venæ comites vel satellites arteriarum.* The large arteries have usually one accompanying vein, and the medium-sized and smaller arteries two, but there are exceptions to this rule. The veins within the skull and spinal canal, the hepatic veins, and the most considerable of those belonging to the bones, run apart from the arteries.

The communications or anastomoses between veins of considerable size, are more frequent than those of arteries of equal magnitude.

Structure.—The veins have much thinner coats than the arteries, and collapse when cut across or emptied; whereas a cut artery presents a patent orifice. But, notwithstanding their comparative thinness, the veins possess considerable strength, more even, according to some authorities, than arteries of the same calibre. The number of their coats has been differently reckoned, and the tissues composing them differently described by different writers, and this discrepancy of statement is perhaps partly due to the circumstance that all veins are not perfectly alike in structure. In most veins of moderate size, three coats may be distinguished, which, as in the arteries, have been named external, middle, and internal.

Internal coat.—This is less brittle than that of the arteries, and therefore admits of being more readily peeled off without tearing; but, in other respects, the

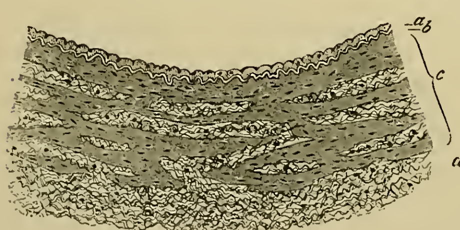


Fig. 425.—TRANSVERSE SECTION OF PART OF THE WALL OF ONE OF THE POSTERIOR TIBIAL VEINS (MAN). (E. A. S.)

a, epithelial and subepithelial layers of inner coat; *b*, elastic layers of inner coat; *c*, middle coat consisting of irregular layers of muscular tissue, alternating with connective tissue, and passing somewhat gradually into the outer connective tissue and elastic coat, *d*.

two are much alike. It consists of an *endothelium*, a *subendothelial connective tissue layer*, and an *elastic layer* (fig. 425, *a*, *b*).

The endothelium of the veins is similar in character to that of the arteries, but the cells are shorter and broader. The subendothelial layer is less developed in most veins than in the arteries, and indeed is absent altogether in many. It is better marked in some of the medium-sized veins than in the larger trunks. The elastic tissue of the inner coat occurs as dense lamelliform networks of longitudinal elastic fibres, and but seldom as fenestrated membranes. Longitudinal muscular bundles, as well as isolated contractile cells, are found in the inner coat of some veins.[1]

Middle coat.—This tunic is thinner than that of the arteries, and has a much larger mixture of white connective tissue. It is pervaded by an elastic network, but this is less conspicuous in the veins than in the arteries. In the veins of the limbs (especially the upper limb) and in those of some other parts, the muscular

[1] Veins which are apparently healthy, sometimes exhibit here and there well-marked thickenings of the inner coat; these thickenings may represent rudimentary valves (Bardeleben).

fibre-cells have for the most part as in the arteries a transverse direction, although the layer which they form is not everywhere complete, being separated into bundles by the intervention of connective tissue (fig. 425, *c*). But in many veins some of the innermost fibres of the middle coat take a longitudinal course. This is the case with the iliac, crural, branches of the mesenteric, umbilical of the fœtus, and other veins (Eberth).

In many of the larger veins the middle coat is less developed, especially as regards its muscular fibres, but in such cases the deficiency may be supplied by muscularity of the outer coat. The middle coat is wanting altogether in the thoracic part of the inferior vena cava, but is well marked in the hepatic part : in the part below the liver the muscularity of the middle coat is less marked. In the internal and external jugular veins there is but a slight development of the muscular tissue.

External coat (fig. 425, *d*).—This is often thicker than the middle coat ; but the line of junction between them is not sharply marked. It consists of dense areolar tissue and longitudinal elastic fibres. In certain large veins, as was first pointed out by Remak, this coat contains a considerable amount of plain or non-striated muscular tissue. Thus the muscular elements are well marked in the whole extent of the abdominal cava, in which they form a longitudinal network, occupying the inner part of the external coat ; and they may be traced into the renal, azygos, spermatic and external iliac veins. The muscular tissue of the external coat is also well developed in the trunks of the hepatic veins and in that of the vena portæ, whence it extends into the splenic and superior mesenteric. It is found also in the axillary vein.

Other veins present peculiarities of structure, especially in respect of muscularity, as follows. 1. The striated muscular tissue of the auricles of the heart is prolonged for some way on the adjoining part of the venæ cavæ and pulmonary veins. 2. The (plain) muscular tissue is largely developed in the veins of the gravid uterus, in which, as well as in some other veins, it is described as being present in all three coats, and as having for the most part a longitudinal arrangement. 3. On the other hand, muscular tissue is wanting in the following veins, viz., *a*, those of the maternal part of the placenta ; *b*, most of the veins of the pia mater ; *c*, the veins of the retina ; *d*, the venous sinuses of the dura mater ; *e*, the cancellar veins of the bones ; *f*, the venous spaces of the corpora cavernosa. In most of these cases the veins consist merely of an epithelium (endothelium) and a layer or layers of connective tissue more or less developed ; in the corpora cavernosa the epithelium is applied to the trabecular tissue. It may be added that in the thickness of their coats the superficial veins surpass the deep, and the veins of the lower limbs those of the upper.

The coats of the veins are supplied with nutrient vessels, *vasa vasorum*, in the same manner as those of the arteries. In some of the larger veins they penetrate into the middle coat and even approach the inner surface. Nerves are distributed to them in the same manner as to the arteries, but in far less abundance.

Valves.—Most of the veins are provided with valves, a mechanical contrivance adapted to prevent the reflux of the blood. The valves are formed of semilunar folds of the internal coat, strengthened by included connective tissue, and projecting into the vein. Most commonly two such folds or flaps are placed opposite each other (fig. 426, A) ; the convex border of each (which, according to Haller, forms a parabolic curve) is connected with the side of the vein ; the other edge is free, and points towards the heart, or at least in the natural direction of the current of the blood along the vessel, and the two flaps incline obliquely towards each other in this direction. Moreover the wall of the vein immediately on the cardiac side of the curved line of attachment of the valves, is dilated into a pouch or *sinus* (fig. 426, B), so that, when distended with blood or by artificial injection, the vessel bulges out on each side, and thus gives rise to the appearance of a knot or swelling

wherever a valve is placed (as in fig. 426, c). From the above description, it is plain that the valves are so directed as to offer no obstacle to the blood in its onward flow, but that, when from pressure or any other cause it is driven back-

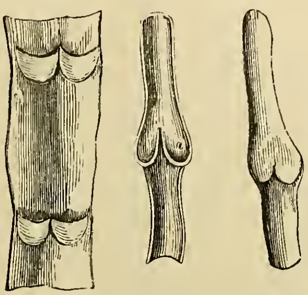


Fig. 426.—Diagram showing valves of veins. (Sharpey.)

A. Part of a vein laid open and spread out, with two pairs of valves. B. Longitudinal section of a vein, showing the apposition of the edges of the valves in their closed state. C. Portion of a distended vein, exhibiting a swelling in the situation of a pair of valves.

wards, the refluent blood, getting between the dilated wall of the vein and the flaps of the valve, will press them inwards until their edges meet in the middle of the channel and close it up.

The epithelium cells differ in shape and arrangement upon the two surfaces of the valves. On the side which faces inwards, and past which the current of blood flows, the cells are elongated in the direction of the current, whereas upon the opposite side which, when the valves are thrown back, faces the wall of the vein, the cells are elongated transversely. The main substance of the valve is formed by bundles of connective tissue, which have for the most part a transverse arrangement, and between which a few elastic fibres are seen. The tissue is covered on each surface by a prolongation of the inner coat of the vein, the covering being much thicker on the inner than on the outer surface. The valve is thinner close to its attachment than elsewhere. At its base a few transverse muscular fibres are sometimes seen, prolonged into it from the middle coat.

The valvular folds are usually placed in pairs as above described: in the veins of the horse and other large quadrupeds three are sometimes found ranged round the inside of the vessel; but this rarely occurs in the human body. On the other hand the folds are placed singly in some of the smaller veins, and in large veins single valvular folds are not unfrequently placed over the openings of smaller entering branches; also in the right auricular sinus of the heart there is a single crescentic fold at the orifice of the vena cava inferior, and another more completely covering the opening of the principal coronary vein.

Many veins are destitute of valves. Those which measure less than $\frac{1}{12}$th of an inch (about 2 millimeters) in diameter rarely, if ever, have them. In man, valves are wanting in the superior and inferior venæ cavæ, in the trunk and branches of the portal vein (except its gastric tributaries, Koeppe), in the hepatic, renal and uterine veins; also in the spermatic (ovarian) veins of the female. In the male, these last-mentioned veins have valves in their course, and in each sex a little valve is occasionally found in the renal vein, placed over the entrance of the spermatic or ovarian. The pulmonary veins, those within the cranium and vertebral canal, and those of the cancellated texture of bone, as well as the trunk and branches of the umbilical vein, are also without valves. In the azygos and intercostal veins valves are not generally found, and when present are few in number. On the other hand, they are numerous in the veins of the limbs (and especially of the lower limbs), which are much exposed to pressure in the muscular movements or from other causes, and have often to support the blood against the direction of gravity. No valves are met with in the veins of reptiles and fishes, and not many in those of birds.

SMALLER ARTERIES AND VEINS AND CAPILLARIES.

That the blood passes from the extreme arteries into the veins was a necessary part of the doctrine of the circulation, as demonstrated by Harvey, in 1628; but

the mode in which the passage takes place was not ascertained until some time after the date of his great discovery. The finding of the capillary vessels, and of the course of the blood through them, was in fact one of the first fruits of the use of the microscope in anatomy and physiology, and was reserved for Malpighi (in 1661).

When the web of a frog's foot is viewed through a microscope of moderate power (as in fig. 427), the blood is seen passing rapidly along the small arteries, and thence more slowly through a network of finer channels, by which it is conducted into the veins. The small vessels interposed between the finest branches of the arteries and the commencing veins, are the capillary vessels. The course of the blood in them may be conveniently seen also in the lungs or mesentery of the frog, in the external gills and tail of tadpoles ; in the tail of small fishes ; in the mesentery of small quadrupeds ; and generally, in short, in the transparent vascular parts of animals which can be brought under the microscope. These vessels can also be demonstrated by means of fine injections of coloured material, not only in membranous parts, such as those above mentioned, but also in more thick and opaque tissues, which can be subsequently rendered transparent.

Fig. 427. — Capillary blood-vessels in the web of a frog's foot, as seen with the microscope (after Allen Thomson).
The arrows indicate the course of the blood.

The capillary vessels of a part are most commonly arranged in a network, the branches of which are of nearly uniform size, though not all strictly equal ; and thus they do not divide into smaller branches like the arteries, or unite into larger ones like the veins ; but the diameter of the tubes, as well as the shape and size of the reticular meshes which they form, differs in different textures. Their prevalent size in the human body may, speaking generally, be stated at from $\frac{1}{3500}$ to $\frac{1}{2000}$ of an inch, as measured when naturally filled with blood. But they are said to be in some parts considerably smaller, and in others larger than this standard : thus, Weber measured injected capillaries in the brain, which he found to be not wider than $\frac{1}{4700}$ of an inch, and Henle has observed some still smaller,—in both cases apparently smaller than the natural diameter of the blood-corpuscles. The capillaries, however, when deprived of blood, probably shrink in calibre immediately after death : and this consideration, together with the fact that their distension by artificial injection may exceed or fall short of what is natural, should make us hesitate on such evidence to admit the existence of vessels incapable of permitting the red corpuscles of the blood easily to pass through them. The diameter of the capillaries of the marrow of the bones is stated to be $\frac{1}{1200}$ of an inch. In other parts, their size varies between the extremes mentioned : it is small in the lungs, and in muscle ; larger in the skin and mucous membranes. The extreme branches of the arteries and veins in certain parts of the synovial membranes are connected by capillary loops, which are considerably dilated at their point of flexure, and dilatations are also found upon the transverse capillaries of the red muscles of the rabbit.

There are differences also in the size or width of the meshes of the capillary network in different parts, and consequently in the number of vessels distributed in a given space, and the amount of blood supplied to the tissue. The network is very close in the lungs and in the choroid coat of the eye, and comparatively close in muscle, in fat, in the skin, and in most mucous membranes, also in glands and secreting structures, and in the grey part of the brain and spinal cord. On the other hand, it has wide meshes and comparatively few vessels in the ligaments, tendons,

and other allied textures. In infants and young persons, the tissues are comparatively more vascular than in after-life.

The figure of the capillary network is not the same in all textures. In many cases the shape of the meshes seems accommodated to the arrangement of the elements of the tissue in which they lie. Thus in muscle, nerve, and tendon, the meshes are long and comparatively narrow, and run conformably with the fibres and fasciculi of these textures. In other parts, as in the lungs, in fat, and in secreting glands, the meshes are rounded or polygonal, with no one dimension greatly predominating. In the papillæ of the skin and mucous membranes, the vessels of the network are often drawn out into prominent simple or ramified loops.

The smallest arteries and veins pass by gradual transition into the capillary vessels, and their finest offsets approach very near to these in structure ; these may therefore be conveniently considered along with the capillary vessels.

Structure of the capillaries.—The wall of the capillaries proper is formed entirely of a simple epithelial layer, composed of flattened lanceolate cells joined edge to edge, and continuous with the corresponding layer which lines the arteries

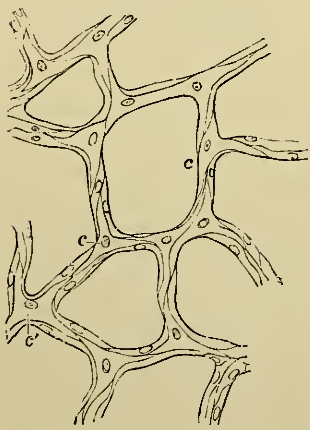


Fig. 428.—Capillary vessels from the bladder of the cat, magnified (after Chrzonszczewsky).

The outlines of the cells are stained by nitrate of silver.

and veins. The outlines of the cells or their lines of junction one with another may be made apparent by nitrate of silver (fig. 428) ; while the nuclei, which show a well-marked network of karyoplasm, may be brought into view by logwood or carmine. Commonly there are not more than two or three such cells in the cross section of a capillary. At the points of junction of the capillaries the cells are usually broader and not spindle-shaped, but radiate, with three or four pointed branches fitting in between the cells of the three or four adjoining vessels which meet at the spot (fig. 428, *c*, *c*, *c'*).

In capillaries which have been submitted to the action of nitrate of silver, there is here and there to be seen between the cells of the capillary wall an increase in amount of the intercellular substance, appearing as an enlargement of the fine line of the silver deposit. To these gaps in the capillary wall, which however are closed by intercellular substance, J. Arnold has applied the term " stigmata ; " they are analogous to the " pseudo-stomata " found between the epithelium-cells of a serous membrane. It is probable that the white blood corpuscles, when migrating from the blood-vessels, pass between the epithelium-cells, especially in the situation of the stigmata.

Branched cells of the surrounding areolar tissue are found connected intimately with the cells forming the capillary wall. This connection occurs almost everywhere, but it is more obvious in parts which are pervaded by a supporting network of retiform connective tissue, such as the substance of the lymphatic glands, the solitary and agminated intestinal glands and adjacent mucous membrane, where the small vessels and capillaries may even obtain a continuous covering from the reticulating processes of the cells. This coating has been named by His, *adventitia capillaris*.

Outgrowths from the capillary wall have been described by Stricker as occurring not only in the progress of development, in the manner to be afterwards detailed, but also in the fully developed capillaries of the frog ; and contraction both of the whole capillary wall and also of the individual cells of young capillary vessels has been described (Stricker, Tarchanoff), but it is not known whether the walls of the capillaries of the adult mammal possess any appreciable contractility.

Structure of the small arteries and veins.—In vessels a little larger than the capillaries, there is added outside the epithelial layer, a layer of plain

muscular tissue, in form of the usual long contractile fibre-cells, which are directed across the length of the vessel. The elongated nuclei of these cells may be brought into view by means of acetic acid or by staining fluids (fig. 430). This layer corresponds with the middle coat of the larger vessels. In the smallest vessels in which it appears the muscular cells are few and apart, and a single long cell may turn spirally round the tube (Lister) ; in larger vessels, especially those of

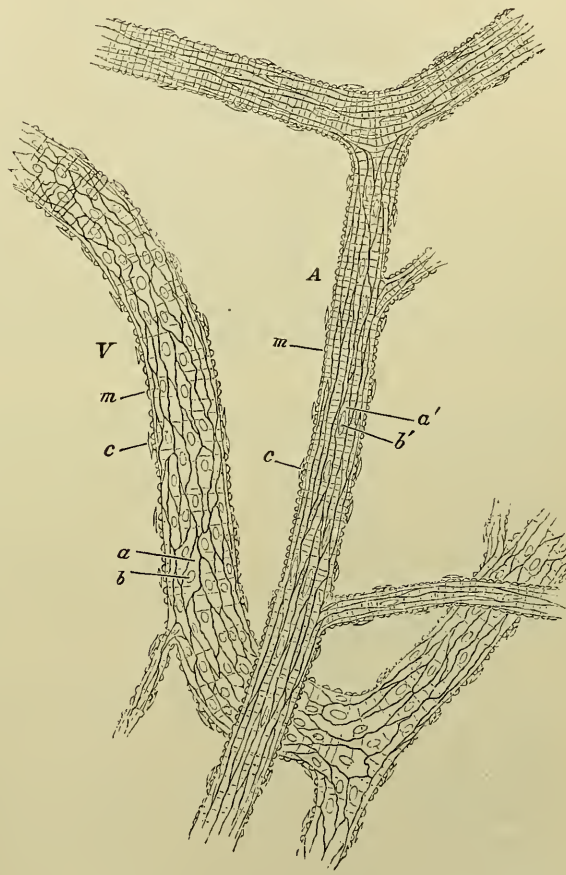


Fig. 429.—A SMALL ARTERY A, AND VEIN V, FROM THE SUBCUTANEOUS CONNECTIVE TISSUE OF THE RAT. TREATED WITH NITRATE OF SILVER. 175 DIAMETERS. (E. A. S.)

a, *a'*, epithelium-cells with *b*, *b'*, their nuclei ; *m*, *m*, transverse markings due to staining of substance between the muscular fibre-cells ; *c*, *c*, nuclei of connective tissue corpuscles attached to exterior of vessel.

the arterial system, the muscular cells are more closely arranged. Outside the muscular coat is the areolar or connective tissue coat, containing fibres and connective tissue corpuscles, with longitudinally placed nuclei.

In vessels of $\frac{1}{60}$ of an inch in diameter, or even less, the elastic layers of the inner coat may be discovered (fig. 430, A, δ), in the form generally of homogeneous or fenestrated membrane, more rarely of longitudinal reticulating elastic fibres. The small veins differ from arteries of corresponding size, chiefly in the inferior development of their muscular tissue ; the lining cells of the arteries also are very much longer and narrower than those of the veins. These differences, as well as the comparative size of corresponding vessels, are well shown in the accompanying figures (429 and 430).

The only open communication between the arteries and the veins, is by means of capillary vessels as above described, unless in the maternal part of the placenta and in the interior of erectile organs, in which small arteries may open directly into wide venous cavities without the intervention of capillaries. Moreover, in the spleen the arterial capillaries do not at once pass into the commencements of the veins, but open into the interstices of the organ, from which the minute veins collect the blood.

But it would appear that in certain parts small arteries may pass into small veins without the intervention of true capillaries (Sucquet, Hoyer).

Arterial glands.—At the upper end of the common carotid (*carotid gland*) and in front of the apex of the coccyx (*coccygeal gland*, Luschka), are found small solid-looking bodies of a

somewhat glandular appearance, but composed almost entirely of a plexus of minute arteries, which are derived in the one case directly from the carotid, in the other from the middle sacral. The plexiform vessels are invested by one or more layers of granular polygonal cells, apparently like those found in the interstitial tissue of some other organs (testis, ovary,

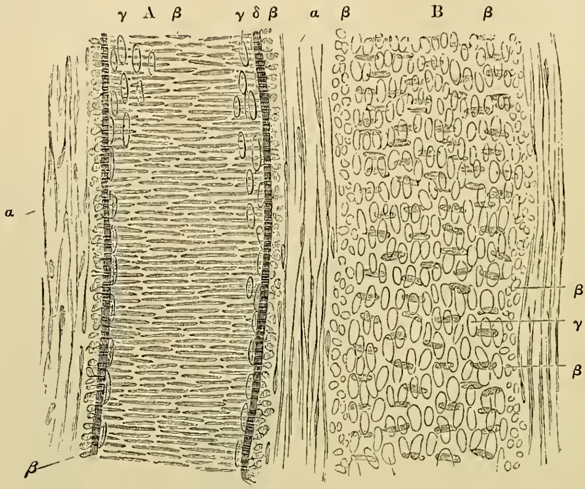


Fig. 430.—A SMALL ARTERY A, WITH A CORRESPONDING VEIN B, TREATED WITH ACETIC ACID, AND MAGNIFIED 350 DIAMETERS (after Kölliker).

α, external coat with elongated nuclei ; β, nuclei of the transverse muscular tissue of the middle coat (when seen endwise, as at the sides of the vessel, their outline is circular) ; γ, nuclei of the epithelium-cells ; δ, elastic layers of the inner coat.

thyroid, suprarenal bodies). The whole is invested by connective tissue, which also penetrates between the vessels of the so-called gland, and itself contains numerous granular cells. The true nature and function of these peculiar structures is entirely unknown, but they are probably of embryological significance.

DEVELOPMENT OF BLOOD-VESSELS.

The first vessels which appear in the ovum are formed in the mesoblast, and the process subsequently goes on in the same layer and in its derivatives in all parts of the animal body. New vessels, also, are formed in the healing of wounds, in the restoration of lost parts, and in the production of adventitious growths. The process is in every case essentially the same.

The first vessels of the embryo, both of the chick and mammal, are formed in the vascular area, and originate from some of the cells of the mesoblast in that situation (fig. 431). Vacuoles are formed within the cells, and as they increase in size run together, and a cavity filled with fluid is in this way produced in the interior of the cell. The nucleus of the cell has meanwhile become multiplied, while blood-corpuscles are formed within the cell-cavity in the manner already described in connection with the blood (p. 217). The cells, whilst these changes are going on, increase largely in size, especially in the chick, where they form vesicles (fig. 432), visible to the naked eye as minute reddish specks, which have been known since the time of Pander as "blood-islands." The cells are united to one another by their processes, and after a time the cavities become extended into the cell-processes, so that a network of vessels is by this means produced.

The wall of these primary vessels is therefore composed at first merely of the protoplasm of the original embryonic cells with nuclei, derived by division from the

original nuclei of those cells, imbedded in it here and there. Subsequently the protoplasm becomes differentiated around the nuclei into the flattened cells which

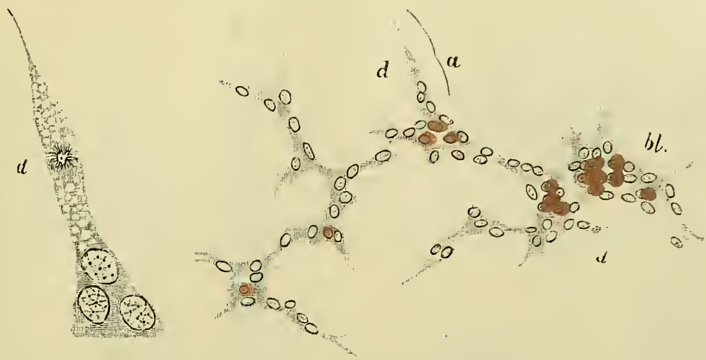


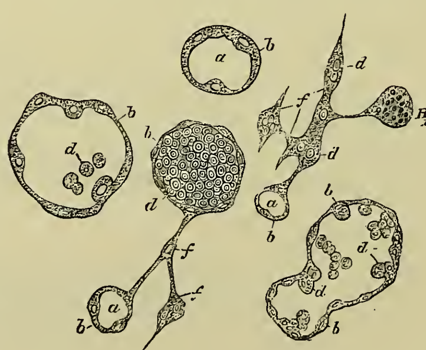
Fig. 431.—Part of the network of developing blood-vessels in the vascular area of the guinea-pig. (E. A. S.)

bl, blood-corpuscles becoming free in an enlarged and hollowed-out part of the network. The smaller figure on the left represents *a* of the larger figure, more highly magnified, showing the vacuolation of the cell; *d*, a nucleus within it undergoing division.

compose the wall of the capillaries, and which form the lining membrane of the arteries and veins. The remaining coats of the larger vessels are developed later,

Fig. 432.—Cells from middle layer of chick's blastoderm undergoing development into blood-vessels. Magnified. (Klein.)

a, cavity of cell; *b*, wall of cell; *f*, *f*, cells not yet hollowed out; *d*, blood-corpuscles.



from other cells which apply themselves to the exterior of the previously simple endothelial tubes and produce the plain muscular and other tissues of which those coats consist.

Within the body of the embryo, vessels are formed in like manner from cells within the connective tissue, especially in rapidly growing vascular organs like the liver. One of the most favourable objects for the study of the development of the blood-vessels and their contained blood-corpuscles is afforded by the subcutaneous tissue of the new-born rat, especially those parts in which fat is being deposited.

Here we may observe that many of the connective tissue corpuscles are much vacuolated, and that the protoplasm of some of them has a decided reddish tinge (fig. 433, *h*). In others the red matter has become condensed in the form of globules within the cells (*h'*, *h''*, &c.), varying in size from minute specks to spheroids of the diameter of a blood-corpuscle, or more. At some parts the tissue is completely studded with these cells, each containing a number of such spheroids, and forming, as it were, "nests" of blood-corpuscles or minute "blood-islands." The cells become elongated and pointed at their ends, sending out processes also to unite with neighbouring cells. At the same time the vacuoles in their interior become enlarged, and coalesce to form a cavity within the cell (fig. 434, *a*), in which the

reddish globules, which are now becoming disk-shaped (b), are found. Finally the cavity extends through the cell-processes into those of neighbouring cells and into those sent out from pre-existing capillaries (fig. 434, c), but a more or less extensive

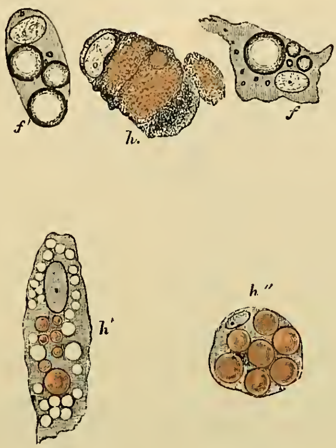


Fig. 433.—Commencing development of angioblastic connective tissue cells into blood-vessels. From the subcutaneous tissue of the new-born rat. (E. A. S.)

h, a cell containing hæmoglobin in a diffused form in the protoplasm ; h', one containing coloured globules of varying size, and vacuoles ; h'', a cell filled with coloured globules of nearly uniform size ; f, f', developing fat cells.

Fig. 434.—Further development of connective tissue cells into capillary blood-vessels. (E. A. S.)

a, an elongated cell with a cavity in its protoplasm occupied by fluid and by blood-corpuscles which are still globular ; b, a hollow cell the nucleus of which has multiplied. The new nuclei are arranged around the wall of the cavity, the corpuscles in which have now become discoid ; c, shows the mode of union of a "hæmapoietic" cell, which in this instance contains only one corpuscle, with the prolongation (bl) of a previously existing vessel. a, and c, from the new-born rat ; b, from the fœtal sheep.

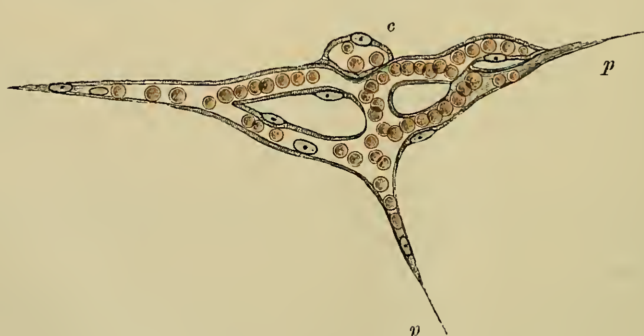


Fig. 435.—Isolated capillary network formed by the junction of several hollowed-out cells, and containing coloured blood-corpuscles in a clear fluid.

c, a hollow cell the cavity of which does not yet communicate with the network ; p, p, pointed cell-processes, extending in different directions for union with neighbouring capillaries.

capillary network is often formed long before the connection with the rest of the vascular system is established (fig. 435). Young capillaries do not exhibit the well-known lines when treated with nitrate of silver, for the differentiation of the hollowed

cells and cell-processes into flattened cellular elements is usually a subsequent process.

The mode of extension of the vascular system in growing parts of older animals, as well as in morbid new formations, is quite similar to that here described, except that blood-corpuscles are not developed within the cells which are forming the blood-vessels.

The blood-vessels may be said to increase in size and capacity in proportion to the demands made on their service. Thus, as the uterus enlarges in pregnancy, its vessels become enlarged, and when the main artery of a limb is tied, or otherwise permanently obstructed, collateral branches, originally small and insignificant, augment greatly in size, to afford passage to the increased share of blood which they are required to transmit, and by this adaptation of them to the exigency, the circulation is restored. In such cases, an increase takes place in length, as well as in diameter, and accordingly the vessels very commonly become tortuous.

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[1] Epstein's paper may especially be consulted for many details regarding the differences of structure of different veins, as well as for references to the older literature of this subject.

LYMPHATIC SYSTEM.

Under this head are included not only the vessels specially called lymphatics or absorbents, together with the glands belonging to them, but also those named lacteal or chyliferous, which form part of the same system, and differ in no respect from the lymphatics, save that they not only carry lymph like those vessels, but are also employed to take up the chyle from the intestines during the process of digestion and convey it into the blood. The serous and synovial membranes may also be conveniently described along with the lymphatic system, since they are—especially the serous membranes—in close relationship to the lymphatics.

A system of lymphatic vessels is superadded to the sanguiferous in all classes of vertebrated animals, but this is not the case in the invertebrata ; in many of these, the sanguiferous vessels convey a colourless or nearly colourless blood, but no additional class of vessels is provided for conveying lymph or chyle.

Distribution.—In man and those animals in which they are present, the lymphatic vessels are found in nearly all the textures and organs which receive blood ; the exceptions are few, and with the progress of discovery may yet possibly disappear. It is, however, with the connective tissue of the several textures and organs that the lymphatics are most intimately associated ; indeed, as we shall immediately have occasion to notice, these vessels may be said to take origin in spaces in that tissue. The larger lymphatic trunks usually accompany the deeply-seated blood-vessels ; they convey the lymph from the plexuses or sinuses of origin towards the thoracic duct. The principal lymphatic vessels of a part exceed the veins in number but fall short of them in size ; they also anastomose or intercommunicate with each other much more frequently than the veins alongside of which they run.

It not unfrequently happens that a lymphatic vessel or a close interlacement of lymphatic vessels, may ensheath an artery or vein either partially or wholly. In this case the lymphatic is termed " perivascular."

Origin.—Two modes of origin of lymphatic vessels are described, viz., the *plexiform* and the *lacunar* or *interstitial*, but no sharp line of distinction can be drawn between them, the difference depending chiefly upon the nature of the tissue or organ to which the lymphatics are distributed. Thus in flat, membranous or expanded parts, the lymphatic vessels usually form a network which is situated either in a single plane, as in many parts of the serous membranes, or in two or more planes united by intervening vessels, as in the skin and some mucous membranes. In the latter case the strata are generally composed of finer vessels, and form a closer network the nearer they are to the surface of the membrane in which they are distributed, but even the most superficial and finest network is composed of vessels which are larger than the sanguiferous capillaries.

The lymphatics of origin are often very irregular in size and shape (fig. 436, *b*, *c*). In them the lymph is collected, and it is conveyed away from the tissues and organs by more regular vessels provided with valves (fig. 436, *a*), which again combine to form larger lymphatic trunks.

Here and there vessels are seen joining the plexuses of origin which arise in the tissue by a blind and often irregular extremity. A long-known and well-marked example of such a mode of commencement is to be found in the lacteals of the intestinal villi, which, although they form networks in the larger and broader villi, arise in others by a single vessel beginning with a blind or closed extremity at the free end of the villus, whence it sinks down to join the general plexus of the intestinal membrane.

On the other hand in the more solid organs the lymphatic vessels occupy the interstices of the organ, and in many cases lose in great measure their character of distinct tubular canals, and appear simply as cleft-like spaces ; these are, however, always bounded by an endothelial layer, like that which lines the lymphatic vessels elsewhere.

The lacunar mode of origin of lymphatics was first described in the testicle by

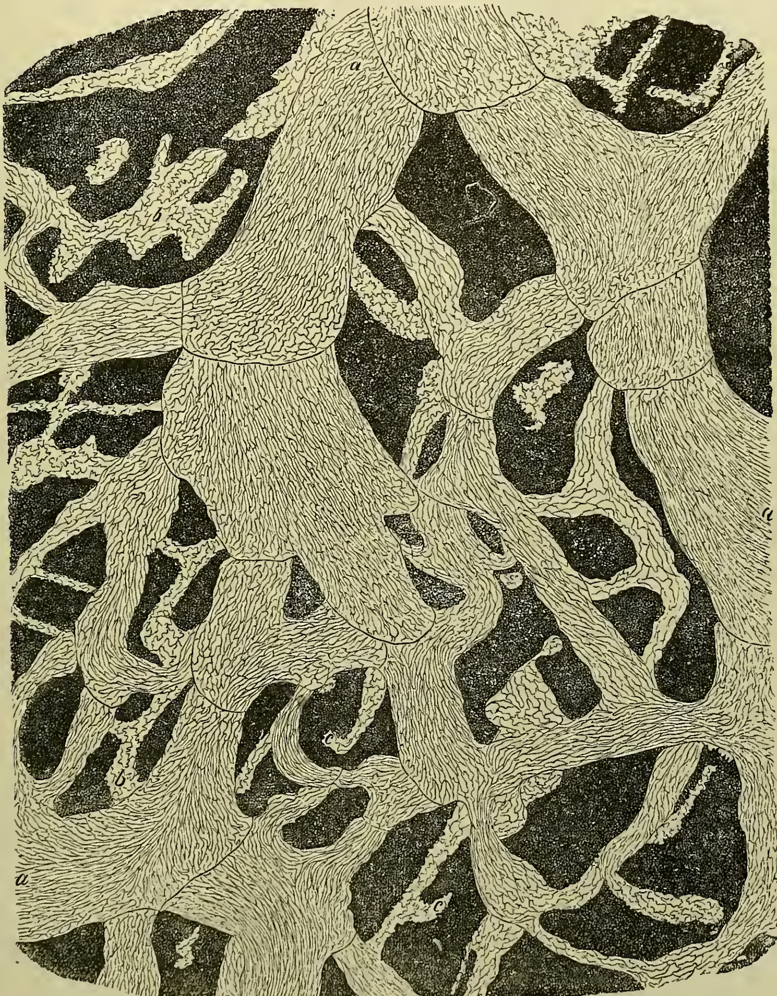


Fig. 436.—LYMPHATIC PLEXUS OF CENTRAL TENDON OF DIAPHRAGM OF RABBIT, PLEURAL SIDE. (Klein.) MAGNIFIED.

a, larger vessels with lanceolate cells and numerous valves ; *b*, *c*, lymphatics of origin, with wavy-bordered cells. Here and there an isolated patch of similar cells.

Ludwig and Tomsa, and it is now known to be characteristic of most glandular organs. Occupying everywhere the interstices of the penetrating connective tissue, the lymph bathes the exterior of the tubules or alveoli of the gland, in many parts even separating them from the capillary blood-vessels, so that the exchanges of material between the plasma of the blood and the secreting cells of the gland must be carried on through the intermedium of the lymph in these spaces. A network of

lymphatic spaces is also met with between the anastomosing muscular fibres of the heart.

What may be regarded as a third mode of origin of lymphatics is to be found in the open communications which subsist between the serous cavities and the lymphatic vessels in their walls. These orifices or *stomata*, which will be described with the serous membranes, allow of the passage of lymph from the serous cavities into the lymphatics, so that those cavities may, in a certain sense, be looked upon as large lymph lacunæ. Owing to this communication fluid is not, under normal circumstances, suffered to accumulate in them.

In some of the lower animals the lacunar condition of lymphatics has been long known. Rusconi found that the aorta and mesenteric arteries of amphibia are inclosed in large lymphatic spaces. Johannes Müller recognised the spaces which so extensively separate the frog's skin from the subjacent muscles as belonging to the lymphatic system, and Recklinghausen showed that the subcutaneous lymph-spaces of the frog's leg communicate with lymphatic vessels which envelope the blood-vessels of the foot; also that milk injected into these spaces finds its way into the blood. The lymphatic system, in being thus constituted by lacunæ or interstitial receptacles, so far agrees with the sanguiferous system of crustaceans and insects.

Structure.—In structure the larger lymphatic vessels much resemble the veins, except that their coats are thinner, so thin and transparent indeed that the contained fluid can be readily seen through them. When lymphatics have passed out from the commencing plexuses and lacunæ, they are found to have three coats. The *internal coat* is covered with an epithelial lining (endothelium), consisting of a single layer of flattened nucleated cells, which have mostly an oblong or lanceolate figure, with an indented or bluntly serrated border, by which the adjacent cells fit to each other (fig. 436, *a*). Outside the endothelial layer the inner coat is formed of a layer or layers of longitudinal elastic fibres. The *middle coat* consists of plain muscular tissue disposed circularly, mixed with finely reticulating elastic fibres taking the same direction. Over the dilatations which occur in the vessels beyond each of the valves, the circular disposition of the muscular fibres gives place to a more irregular disposition, taking the form of an intricate interlacement of fibres. The *external coat* is composed mainly of white connective tissue with a sparing intermixture of longitudinal elastic fibres, and some longitudinal and oblique bundles of plain muscular tissue. In the thoracic duct there is a sub-epithelial layer (as in the arteries); and in the middle coat there is a longitudinal layer of white connective tissue with elastic fibres, immediately within the muscular layer. The muscular fibres of the middle coat, although for the most part transverse in direction, are nevertheless many of them oblique or even longitudinal.

The largest lymphatics have blood-vessels ramifying in their outer coat.

The commencing lymphatics or lymphatic capillaries, whether in plexuses or single (as in the villi), have a much simpler structure, their wall being entirely formed of a layer of endothelium either similar in form to those lining the larger vessels or (more frequently) presenting a characteristic waved border like the epidermic cells of grasses and some other plants (fig. 437).

Gaskell has described an attachment of elastic fibres to the walls of smaller lymphatics in some parts, and infers that the patency of the lumen of these vessels may by this means be restored after it has been temporarily obliterated by pressure (or by contraction of the muscular coat).

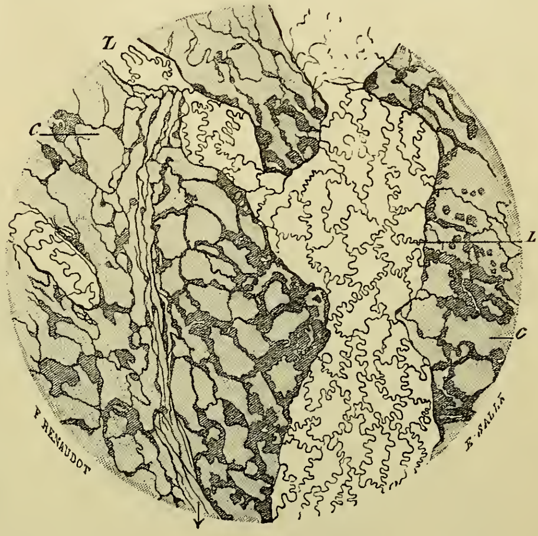
Valves.—The lymphatic and lacteal vessels are furnished with valves serving the same office as those of the veins, and for the most part constructed after the same fashion. They generally consist of two semilunar folds arranged in the same way as in the valves of veins already described, but deviations from the usual structure here

and there occur. A difference is found in the epithelium upon the two surfaces of the valves similar to that which has been noticed in the valves of the veins.

Valves are not present in all lymphatics, but where they exist they follow one another at much shorter intervals than those of the veins, and give to the lymphatics when distended, a beaded or jointed appearance. Valves are placed at the entrance

Fig. 437. —Part of a lymphatic vessel in the pleural covering of the diaphragm. $\frac{110}{1}$. (Ranvier.)

L, L, the lymphatic vessel with characteristic epithelium; *c,* cell-spaces of the connective tissue.



of the lymphatic trunks into the great veins of the neck. They are generally wanting in the reticularly arranged vessels which compose the plexuses of origin already spoken of; so that fluid injected into one of these vessels runs in all directions, so as to fill a greater or a less extent of the plexus, and passes along the separate vessels which issue from it.

The lymphatics of fishes and amphibia are, generally speaking, destitute of valves, and may therefore be injected from the trunks; and valves are much less numerous in the lymphatics and lacteals of reptiles and birds than in those of mammiferous animals.

Relation of the lymphatics of origin to the cells and cell-spaces of the connective tissue.—It has been already stated (p. 233) that the cells of the connective tissue lie in spaces in the ground-substance which they more or less completely fill. These cells and cell-spaces form in many parts an intercommunicating network of varying fineness extending throughout the substance of the tissue (fig. 437, *c*, fig. 438, *d, d,* fig. 439, *c, c*), whilst in other parts the cells acquire a broad flattened form, and joining edge to edge with other similar cells may in this way form an epithelioid patch in the ground substance. Not unfrequently the cells in such a patch take on the wavy border described above as met with in the lymphatics of origin (see the isolated patches in fig. 436). Further, the flattened cells which form the walls of the lymphatics are connected here and there both with the more ramified cells of the tissue (fig. 438, *e*) and with those which form the epithelioid patches, and in silvered preparations they appear to be continuous with one another. The epithelioid patches look in fact like a part of the lymphatic vessels, and are often regarded as such; it must be understood, however, that the spaces here spoken of, whether containing single cells or groups, are not true *vessels,* but merely vacuities in the ground-substance of the tissue containing flattened cells, which do not form a continuous vascular wall. And although the spaces present a very close relation to the lymphatic vessels, they can hardly be considered as actually opening into them by patent orifices, for the lymphatics proper have a complete wall of flattened cells united by a small amount of intercellular substance: at the same time this thin film can offer but a very slight resistance to the passage of fluid from the tissue into the vessel, or even to the passage of leucocytes or migrating cells, which, as is well known, penetrate the at least equally closed wall of the blood-vessels.

It has been a question whether the cell-spaces of the connective tissue are in every case and completely filled by the cells, or whether the spaces may in some cases be either devoid of cells altogether, or but partially occupied by them; so that room is left for the free passage of fluid. On this point we would remark that in many cases it is impossible to observe a difference between the forms of the *cells* as shown by the gold method, and those of the *spaces* as shown by treatment with nitrate of silver, so that in these instances, at least, no open lymph-passage can be said to exist; but in other cases the spaces are relatively larger, and here, no doubt, the part unoccupied by the contained cell may be filled by fluid. In œdematous conditions of the tissue, the cell-spaces become somewhat distended with serous fluid, and then in all cases they appear distinctly larger than the cells. Even where the *Saft-canälchen* or lymphatic canaliculi (which correspond with our cell-spaces) are completely filled

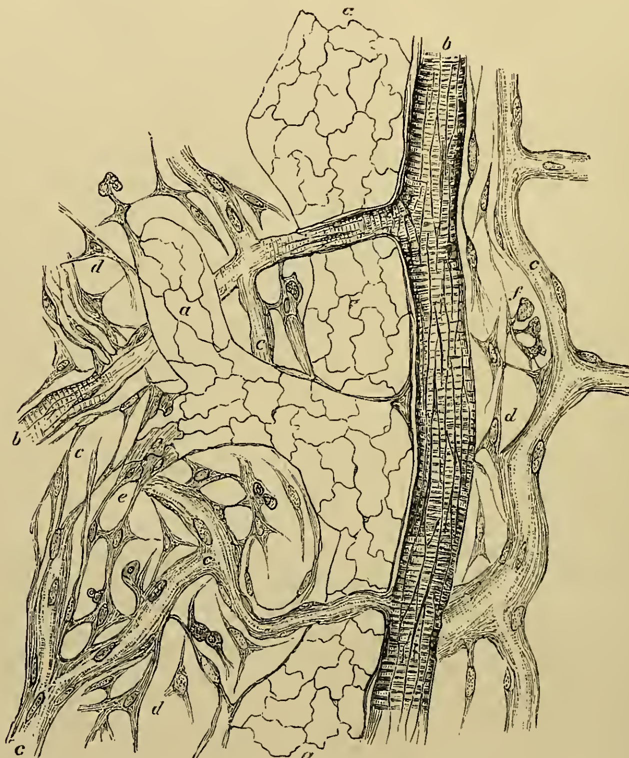


Fig. 438.—Nitrate of silver preparation from rabbit's omentum. (Klein.) Magnified.

a, lymphatic vessel; *b*, artery; *c*, capillaries; *d*, branched cells of the tissue which are seen to be connected both with the capillary walls, and, as at *e*, with the lymphatic. The cells are, in this instance, stained by the nitrate of silver.

by protoplasmic cells, lymph can still readily find its way between the cells and the ground-substance by which they are closely surrounded. In other cases where the cells incompletely fill the cavities, a freer passage is left for both fluid and migratory corpuscles.

A point still more difficult to decide is the existence or not of an open communication between the areolæ of the connective tissue and the lymphatic vessels. The result of the injection of coloured fluids into the meshes of the areolar tissue in many parts would lead to the conclusion that some such communication may really exist, for the injection most generally finds its way into the lymphatics. But it is very difficult to demonstrate such a connection anatomically, and up to the present time it can scarcely be said to be proved. It must be remembered that the ground-substance of the connective tissues is itself by no means impermeable to fluids, nor as we have just stated can it be supposed that the delicate walls of the commencing lymphatics can oppose any material obstacle to the passage of fluid into their cavity.

Terminations of lymphatics.—The absorbent system discharges its contents into the veins at two points, namely, at the junction of the subclavian and internal jugular veins of the left side by the thoracic duct, and at the corresponding part of the veins of the right side by the right lymphatic trunk. The openings, as already remarked, are guarded by valves. It sometimes happens that the thoracic duct divides, near its termination, into two or three short branches, which open separately, but near each other; more rarely, a branch opens to the vena azygos—indeed the main vessel has been seen terminating in that vein. Again it is not uncommon for larger branches, which usually join the thoracic duct, to open independently in the vicinity of the main termination; and this is more apt to happen with the branches

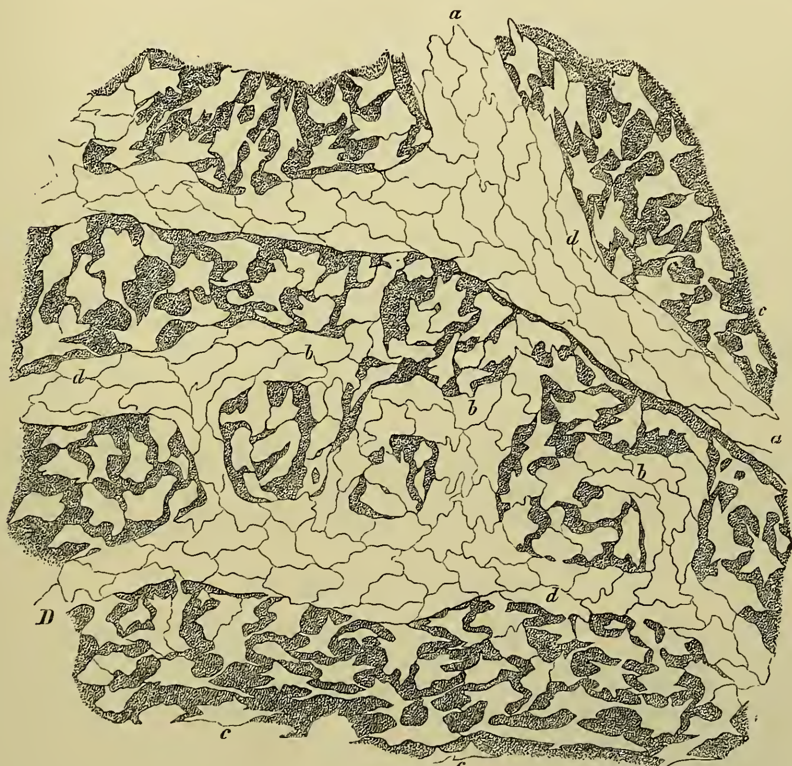


Fig. 439.—Portion of serous membrane of diaphragm (pleural) from the rabbit, treated with nitrate of silver after removal of superficial epithelial layer. (Recklinghausen.)

c, c, cell-spaces of tissue; *d, d,* commencing lymphatic vessels connected at *b, b,* with the cell-spaces.

which usually unite to form the right lymphatic trunk. By such variations the terminations in the great veins are multiplied, but still they are confined in man to the region of the neck; in birds, reptiles, and fishes, on the other hand, communications take place between the lymphatics of the pelvis, posterior extremities and tail, and the sciatic or other considerable veins of the abdomen or pelvis.

Lymphatic hearts.—J. Müller and Panizza, nearly about the same time, but independently of each other, discovered that the lymphatic system of reptiles is furnished, at its principal terminations in the venous system, with pulsatile muscular sacs, which serve to discharge the lymph into the veins. These organs, which are named lymph-hearts, have now been found in all the different orders of reptiles and amphibia, and also in birds, but not in any mammal. In frogs and toads two pairs have been discovered, a

posterior pair, situated in the sciatic region, which pour their lymph into a branch of the sciatic or of some other neighbouring vein, and an anterior more deeply-seated pair, placed over the transverse process of the third vertebra, and opening into a branch of the jugular vein. The parietes of these sacs are thin and transparent, but contain muscular tissue, which here and there appears obscurely striated, decussating in different layers, as in the blood-heart. In their pulsations they are quite independent of the latter organ, and are not even synchronous with each other. In salamanders, lizards, serpents, tortoises, and turtles, only a posterior pair have been discovered, which, however, agree in all essential points with those of the frog. In the goose, and in other species of birds belonging to different orders, Panizza discovered a pair of lymph-sacs opening into the sacral veins, and Stannius has since found that these sacs have striated muscular fibres in their parietes. Nerve-fibres, both dark-bordered and pale, have been observed in the lymph-hearts of the frog, and also nerve-cells in those of the common tortoise (Waldeyer).[1]

Development of lymphatic vessels.—The development of lymphatic capillaries has been studied by Klein in the serous membranes. He finds that the process is similar to that of the development of blood-vessels. A vacuole is formed within one of the cells of the connective tissue, and becomes gradually larger, so as ultimately to produce a cavity filled with fluid, with the protoplasm of the cell thinned out to form the wall of the vesicle thus produced. From this protoplasmic wall portions are said to bud inwards into the cavity, eventually becoming detached as lymph corpuscles ; it is more probable, however, that the lymph corpuscles which are seen in the developing lymphatics have "wandered in," as in the case of the white corpuscles of the blood. Meanwhile the nucleus of the cell has become multiplied, and the resulting nuclei are regularly arranged in the protoplasmic wall, which now exhibits, on treatment with nitrate of silver, the well-known wavy epithelial marking characteristic of the lymphatic capillaries. To form vessels, the vesicles become connected with one another by means of processes into which their cavities extend.

The cells lining these lymphatic vesicles, which are common in the mesogastrium of the frog and toad in the winter season bear, in the female of those animals, cilia directed inwards towards the cavity of the vesicles. As the development into vessels proceeds, the cilia disappear (Klein). Remak, who first noticed these ciliated vesicles, took them for cysts in the membrane.

LYMPHATIC GLANDS.

Lymphatic glands, formerly named also *conglobate glands*, and by modern French writers *lymphatic ganglions*, are small solid bodies placed in the course of the lymphatics and lacteals, through which the contents of these vessels have to pass in their progress towards the thoracic or the right lymphatic duct. These bodies are collected in numbers alongside of the great vessels of the neck, and also in the thorax and abdomen, especially in the mesentery and alongside of the aorta, vena cava inferior, and iliac vessels. A few, usually of small size, are found on the external parts of the head, and considerable groups are situated in the axilla and groin. Some three or four lie on the popliteal vessels, and usually one is placed a little below the knee, but none farther down. In the arm they are found as low as the elbow joint.

The lymph of some lymphatic vessels has to traverse two, three, or even more lymphatic glands before reaching the thoracic duct, whilst, on the other hand, there are lymphatics which enter the thoracic duct without having traversed any gland in their way.

The size of lymphatic glands is very various, some being not much larger than

[1] Müller's description is to be found in the Philosophical Transactions for 1833 ; Panizza's in a special memoir on the Lymphatic System of Reptiles, published in the same year. For a more complete account of the lymphatic hearts of the frog, the reader is referred to the "Leçons d'Anatomie Générale," delivered by Prof. Ranvier in the Collège de France in 1877–78, and published in 1880, and to the "Traité Technique" of the same author, 2nd edition, published in 1889.

a hempseed, and others as large as an almond or a kidney bean, or even larger than this. In shape, too, they present differences, but most of them are round or oval.

The lymphatics or lacteals which enter a gland are named inferent or afferent vessels (*vasa inferentia* seu *afferentia*), and those which issue from it efferent vessels

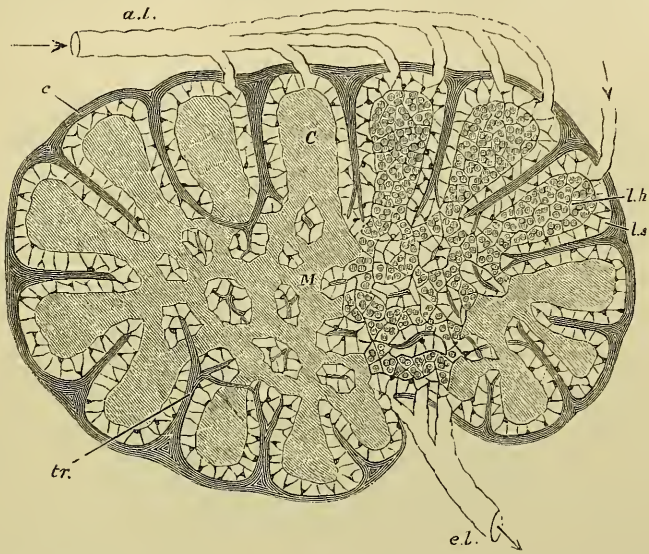


Fig. 440.—DIAGRAMMATIC SECTION OF LYMPHATIC GLAND. (Sharpey.)

a.l, afferent; *e.l*, efferent lymphatics. C, cortical substance. M, reticulating cords of medullary substance. *l.s*, lymph-sinus; *c*, fibrous coat sending trabeculæ, *tr*, into the substance of the gland.

(*vasa efferentia*). The afferent vessels (fig. 440, *a.l*), on approaching a gland, divide into many small branches, which enter the gland; the efferent vessels commonly leave the gland in the form of small branches, and at a little distance

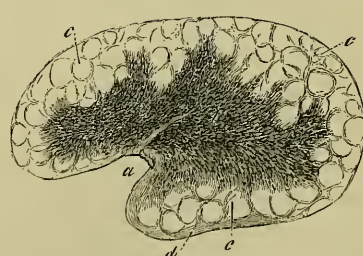


Fig. 441.—SECTION OF A MESENTERIC GLAND FROM THE OX, SLIGHTLY MAGNIFIED. (Kölliker.)

a, hilum; *b*, medullary substance; *c*, cortical substance with indistinct alveoli; *d*, capsule.

beyond it, or sometimes even before issuing from it, unite into one or more trunks (*e. l*), usually larger in size but fewer in number than those of the afferent vessels.

A lymphatic gland is covered externally with a coat (figs. 440, 442, *c*) composed of connective tissue, mixed, in certain animals, with muscular fibre-cells. This coat or capsule dips into the interior of the gland at the place where the larger blood-vessels and the efferent lymphatics pass into and out of the organ; and this part of the gland, which often has a depression or fissure, is named the *hilum* (fig. 441, *a*). The proper substance of the gland consists of two parts, the *cortical* (fig. 440, *C*), and within this the *medullary* (*M*). The cortex occupies all the superficial part of the gland, except the hilum, and in the larger glands may attain a thickness of one or two millimeters. The medullary portion occupies the centre and extends to the surface at the hilum. It is most developed in the inwardly-seated glands, such as the lumbar and mesenteric, whilst in the subcutaneous glands it is more encroached

upon by the connective tissue which enters with the larger blood-vessels at the hilum, and surrounds them, together with the lymph-vessels, in the centre of the gland, so that in these the medullary part is reduced to a layer of no great thickness bounding inwardly the cortical part.

Throughout both its cortical and medullary part the gland is pervaded by a trabecular frame-work which incloses and supports the proper glandular substance.

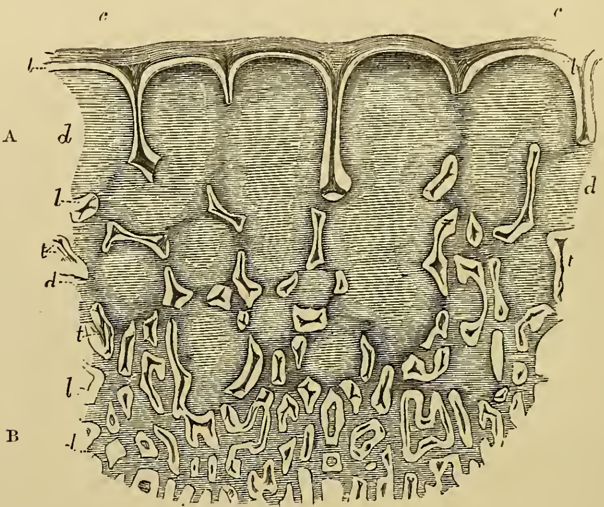


Fig. 442.—Section of a mesenteric gland of the ox (magnified 12 diameters). After His.

The section includes a portion of the cortical part, A, in its whole depth, and a smaller portion of the adjoining medullary part, B ; *c*, *c*, outer coat or capsule sending partitions into the cortical part, eventually forming the trabeculæ, *t*, *t*, which are seen mostly cut across ; *d*, *d*, the glandular substance forming nodules in the cortical part, A, and reticulating cords in the medullary part, B ; *l*, *l*, lymph-sinus or lymph-channel, left white.

The trabeculæ pass inwards from the capsule (fig. 440). They consist, in the ox and most animals, chiefly of plain muscular tissue ; in man, of connective tissue, sparingly intermixed with muscular fibre-cells. In the cortical part they are mostly lamellar in form, and partially divide the cortex up into separate nodules from $\frac{1}{60}$ to $\frac{1}{24}$ of an inch in diameter, which communicate laterally with each other through openings in the imperfect partitions between them (fig. 442, A). On reaching the medullary part the trabeculæ take the form of flattened bands or rounded cords, and by their conjunction and reticulation form a freely intercommunicating mesh-work throughout the interior. (In figure 442 they are represented mostly as cut across.) In the interstices of the framework which is thus formed by the capsule and trabeculæ is included the proper *glandular substance*, which appears as a tolerably firm pulp or parenchyma, composed of lymphoid tissue. Within the cortical part this forms rounded nodules (*cortical nodules or follicles*) (fig. 442, A, *d*) ; in the trabecular meshes of the medullary part it takes the shape of rounded cords (*lymphoid cords*) joining in a corresponding network (fig. 442, B) ; and, as the containing meshes of the framework inter-communicate, so the contained gland-pulp is continuous throughout. But both in the cortical and the medullary parts, a narrow space, left white in the figs. (fig. 440, *l.s* ; 442, *l*, *l*), is left all round the gland-pulp, between it and the trabeculæ, such as would be left had the pulp shrunk away from the inside of a mould in which it had been cast. This space is both a receptacle and a channel of passage for the lymph that goes through the gland ; it is named the *lymph-sinus*, or *lymph-channel*. It is traversed by retiform connective

tissue (fig. 440 ; fig. 443, *r*), the fibres of which are for the most part covered and concealed in the natural condition by ramified cells, and is filled with fluid lymph, containing many lymph-corpuscles, which may be washed out from sections of the gland, so as to show the sinus, while the firmer gland-pulp, which the sinus surrounds, keeps its place. The proper glandular substance is also pervaded and

Fig. 443.—Reticulum from the medullary part of a lymphatic gland. (E. A. S.)

tr, end of a trabecula of fibrous tissue ; *r*, *r*, open reticulum of the lymph-path, continuous with the fibrils of the trabecula ; *r'*, *r'*, denser reticulum of the medullary lymphoid cords. The cells of the tissue are not represented, the figure being taken from a preparation in which only the connective tissue fibrils and the reticulum are stained.

supported by fine retiform tissue (figs. 443, *r'*, 445, *a*), communicating with that of the surrounding lymph-sinus, but marked off from it by somewhat closer reticulation at their mutual boundary, not so close, however, as to prevent fluids, or even

Fig. 444.—End of a fibrous trabecula from the same preparation, showing the continuity of the connective tissue fibrils with the reticulum : highly magnified. (E. A. S.)

tr, trabecula ; *r*, reticulum.

corpuscles, from passing from the one to the other. The gland-pulp is otherwise made up of densely packed lymphoid cells, occupying the interstices of its supporting retiform tissue, and usually exhibiting, especially at its peripheral parts, abundant evidence of the process of division and multiplication by karyokinesis. This lymphoid tissue is traversed by a network of capillary blood-vessels (fig. 445, *d*, *d*), which run throughout the proper glandular pulp, both cortical and medullary, but do not pass into the surrounding lymph-sinus. The lymphoid cells of the glandular pulp are similar in their general appearance to white blood- or lymph-corpuscles, except that their nucleus is relatively larger, and their protoplasm less in amount.

The ramified cells which cover the retiform tissue of the lymph-sinus, often contain a considerable number of pigment-granules, especially in the medulla of the gland. The trabeculæ themselves have a covering of flattened cells, which on the side turned towards the lymph-channel are provided with processes to anastomose with those covering the retiform tissue. The inner surface of the capsule is also lined with flattened cells, which are continuous at the entrance and exit of the lymphatics with the endothelium of those vessels.

Arteries enter and veins leave the gland at the hilum, surrounded, in some

glands, as already said, with a dense investment of connective tissue. The arterial branches go in part directly to the glandular substance, but partly run along the trabeculæ. The former end in the glandular capillary network above-mentioned, from which the veins begin, and tend to the hilum alongside the arteries. The branches which run along the trabeculæ are partly conducted to the coat of the gland to be there distributed; but most of their branches pass to the glandular substance, the connective tissue of the trabeculæ which ensheaths them passing gradually into the lymphoid tissue of the pulp, so that this at first appears as a

Fig. 445.—Section of the medullary substance of a lymphatic gland (ox). 300 diameters. (Recklinghausen.)

a, a, a, follicular or lymphoid cords; *b, b,* trabeculæ; *c,* lymph-sinus; *d, d,* blood-vessels.

sheath to the arterial branch (as in the spleen). The latter soon, however, breaks up into capillaries which ramify in the gland-pulp, supported by its pervading retiform tissue, which forms an additional adventitious coat around the minute vessels.

As to the lymphatics of the gland, the afferent vessels, after branching out upon and in the tissue of the capsule, send their branches through it to open into the lymph-sinuses of the cortex, and the efferent lymphatics begin by fine branches leading from the lymph-sinuses of the medullary part, and forming at the hilum a dense plexus of tortuous and varicose-looking vessels, from which branches proceed to join the larger efferent trunks. The lymph-sinus, therefore, forms a path for the passage of the lymph, interposed between the afferent and efferent lymphatics, communicating with both and maintaining the continuity of the lymph-stream. The afferent and efferent vessels, where they open into the lymph-sinus, lay aside all their coats, except the epithelial lining, which is continued over the trabeculæ and the interior of the capsule.

The chief differences of structure which are seen in lymphatic glands depend upon the relative amount and nature of the framework. Thus whereas in some animals both the capsule and the trabeculæ are strong and muscular, in others they are less developed and contain but little plain muscular tissue. In some animals

the trabeculæ are almost or entirely absent, and the interior of the gland then looks in section like a continuous mass of lymphoid tissue, traversed by lymphatic channels.

It is not unreasonable to presume that, in the proper glandular substance, there is a continual production of lymph-corpuscles, which pass into the lymph-sinus, and that fresh corpuscles are thus added to the lymph as it traverses the gland. This view is supported by the fact, that the corpuscles are found to be multiplying by karyokinesis within the pulp, and are more abundant in the lymph or chyle after it has passed through the glands.

Other organs composed of lymphoid tissue.—Bodies which are similar in structure to lymphatic glands in so far that they are composed of a delicate retiform tissue, the interstices of which are closely packed with lymphoid cells, and are in intimate relation with the lymphatic vessels of the part, occur in many places. Thus, in the serous membranes, rounded nodules are here and there met with, which, as Klein has shown, are developed either around or at one side of an enlarged lymphatic (*perilymphangial nodule*, fig. 446, A), or in some cases even within the vessel (*endolymphangial nodule*, fig. 446, B). The retiform tissue which constitutes the framework of the nodule is connected with the wall of the lymphatic, and lymphoid cells accumulate in the interstices of the retiform tissue, where they multiply and ultimately form a dense mass of lymphoid tissue.

The endolymphangial nodules, although small and simple in structure, closely recall the structure of one of the cortical nodules of a lymphatic gland ; for a path

Fig. 446.—Developing lymphatic (lymphangial) nodules, from the omentum of a guinea-pig. (Klein.)

A, perilymphatic nodule ; *a*, lymphatic vessel ; *c*, part of its epithelial wall, seen in optical section ; *e*, lymph-corpuscles within the vessel ; *b*, lymphoid tissue of the nodule ; *d*, blood-capillaries. B, endolymphatic nodule ; *a*, vein ; *b*, artery ; *c*, capillaries ; *d*, a lymphatic vessel, in which this whole system of blood-vessels is inclosed ; *e*, lymphoid tissue within the lymphatic vessel ; *f*, wall of the lymphatic in optical section.

or channel for the passage of lymph is left between the central accumulation of lymphoid tissue and the wall of the vessel, this path being bridged across by retiform tissue and branched cells ; and along it the lymph must pass very slowly, and come into intimate relation with the tissue of the nodule. In other cases the lymphoid tissue of the serous membranes is less circumscribed, occurring in the form of ill-defined patches or elongated tracts, which lie along the course of the small arteries and veins, receiving from the latter branches which form a capillary network within the tissue.

In mucous membranes, especially that lining the alimentary canal, conspicuous lymphatic nodules are met with in various parts, and here they have been long known. They occur either singly, as in the so-called *solitary glands* of the intestine, or collected into groups as in the *agminated glands* or patches of Peyer, or into thick masses as in the *tonsils*. In most of these cases the nodules are spherical or dome-shaped condensations of the lymphoid tissue which occurs in the substance of the mucous membrane, on the surface of which they may cause a distinct prominence ; they are usually found to be in close relation with the lymphatics of the membrane, being either partially surrounded by a large sinus-like lymphatic, or encircled by a plexus of lymphatic vessels. In the mucous membrane of the bronchial tubes lymphoid nodules are met with which are quite similar to those of the alimentary mucous membrane. In the spleen, tracts of lymphoid tissue, with lymphatics in connexion with them, ensheath the smaller arteries and are dilated at certain points into distinct nodules which have here been long known as the *Malpighian corpuscles of the spleen*. Lastly the *thymus gland* seems to be chiefly composed in the young subject of lymphoid tissue having a more or less nodulated arrangement, although in the adult this organ is usually found to have become transformed into adipose tissue.

It has been shown by Flemming that the nodular formations of lymphoid tissue are in all cases due to the rapid multiplication of cells which is occurring at the spots where they are found; that they represent, in short, foci of multiplication.

The further description of the lymphoid structures will be deferred until the several organs where they occur are systematically treated of.

SEROUS MEMBRANES.

The serous membranes are so named from the apparent nature of the fluid with which their surface is moistened. They lie in cavities of the body which have no obvious outlet, and the chief examples of them are, the *peritoneum*, the largest of all, lining the cavity of the abdomen; the two *pleuræ* and the *pericardium* in the chest ; and the *tunica vaginalis* surrounding each of the testicles within the scrotum.

The arachnoid membrane, which is a delicate connective tissue membrane surrounding the brain and spinal marrow in the bony cavities in which they are contained, was formerly reckoned amongst the serous membranes ; but neither in the details of its structure, in its general disposition, nor in its development does it correspond with the other serous membranes. It is, therefore, no longer classed with them, but will be described with the other membranes investing the brain and spinal cord.

Form and arrangement.—In all cases a serous membrane has the form of a closed sac, one part of which is applied to the walls of the cavity which it lines, the *parietal* portion ; whilst the other is reflected over the surface of the organ or organs contained in the cavity, and is therefore named the *reflected* or *visceral* portion of the membrane. Hence the viscera in such cavities are not contained within the sac of the serous membrane, but are really placed behind or outside of it ; seeming to push inwards the part of the membrane which immediately covers them, some organs receiving in this way a complete, and others only a partial and sometimes very scanty investment.

In passing from one part to another, the membrane frequently forms folds which in general receive the appellation of ligaments, as, for example, the folds of peritoneum passing between the liver and the parietes of the abdomen, but which are sometimes designated by special names, as in the instances of the mesentery, mesocolon, and omentum.

The peritoneum in the female sex, is an exception to the rule that serous mem-

branes are perfectly closed sacs, inasmuch as it has two openings by which the Fallopian tubes communicate with its cavity.

A serous membrane sometimes lines a fibrous membrane, as where the serous layer of the pericardium adheres to its outer or fibrous part. Such a combination is often named a *fibro-serous* membrane.

The inner surface of a serous membrane is free, smooth, and polished ; and, as would occur with an empty bladder, the inner surface of one part of the sac is applied to the corresponding surface of some other part ; a small quantity of fluid, usually not more than merely moistens the contiguous surfaces, being interposed. The parts situated in a cavity lined by serous membrane, being themselves also covered by it, can thus glide easily against its parietes or upon each other, and their motion is rendered smoother by the lubricating fluid.

The outer surface most commonly adheres to the parts which it lines or covers, the connection being effected by means of areolar tissue, named therefore "subserous," which, when the membrane is detached, gives to its outer and previously adherent surface a flocculent aspect. The degree of firmness of the connection is very various : in some parts the membrane can scarcely be separated ; in others its attachment is so lax as to permit easy displacement.

Structure and properties.—Serous membranes are thin and transparent, so that the colour of subjacent parts shines through them. They are tolerably strong,

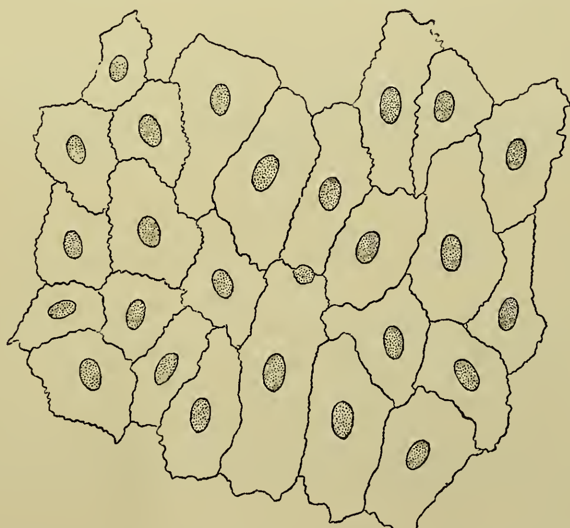


Fig. 447.—Endothelial layer of omentum of rabbit. Nitrate of silver preparation. (E. A. S.)

with a moderate degree of extensibility and elasticity. They are lined on the inner surface by a simple epithelial layer of flattened cells (*endothelium*, fig. 447), each of which contains a round or oval nucleus with one or two nucleoli, and an intranuclear network. The cells have, according to Klein, a comparatively coarse network of minute fibrils embedded in the otherwise clear cell-substance. The outlines of the cells may readily be brought into view by treatment with nitrate of silver. The lines of junction of the cells which are thus made evident, may be straight and even, but are most commonly slightly jagged or sinuous. Here and there between the cells apertures are to be seen, which are of two kinds. The smaller, which are also the more numerous, are occupied either by an accumulation of the intercellular

substance or by processes which are sent up to the surface of the membrane from more deeply lying cells (*pseudostomata* of Klein and Burdon-Sanderson): the larger ones, on the other hand, are true apertures (*stomata*), which are surrounded by a ring of small cubical cells (fig. 449, *s*, *s'*), and open into a subjacent lymphatic vessel, either directly or by the medium of a short canal lined with similar cells. The surface cells of the serous membrane are not everywhere uniform in size, but patches are here and there met with in which they are smaller and more granular in appearance and it is in these parts that the stomata and pseudo-stomata are more frequently seen (figs. 448, 449). The epithelium-cells of the membrane often

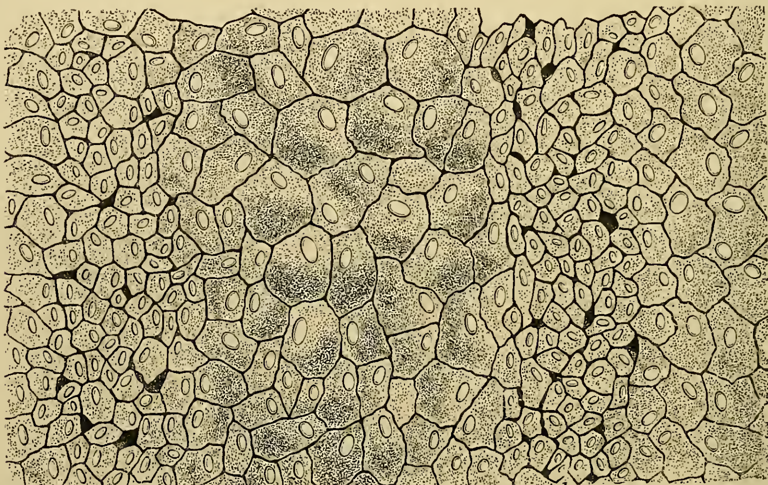


Fig. 448.—Portion of endothelium of peritoneum from the under surface of the rabbit's diaphragm. (Klein.)

a, larger cells; *b*, smaller ones, with here and there a pseudostoma between.

present a somewhat radiated aspect near the stomata, the silver lines converging towards the orifice. According to Klein, it is not unfrequent to find evidences of proliferation, especially in the neighbourhood of the stomata and pseudo-stomata, cells being met with containing two or even many nuclei, and others which are being budded off from the cells of the membrane. Since, however, these statements depend on observations which were made before the importance of the karyokinetic figures as a guide to cell-multiplication was recognised, it is important that they should be repeated.

The stomata were discovered in the peritoneal covering of the central tendon of the diaphragm by Recklinghausen, who found that milk-globules could be made to pass through them into the lymphatics. Similar apertures were found by Ludwig and Dybkowsky in the pleura of mammals, and by Schweigger-Seidel and Dogiel in the septum between the peritoneal cavity of the frog and the great lymph-sac (cisterna magna) behind it. They have since been discovered on the omentum by Klein, and have also been recognised in the pericardium.

The substance of the membrane underneath the endothelium is composed of a connective tissue ground-substance in which is a variable amount of fibres, both white and elastic; the latter in many serous membranes, as remarked by Henle, are principally collected into a reticular layer near the surface. The bundles of white fibres are also arranged in a reticular manner, frequently uniting with one another, and the meshes of the reticulation which they form are occupied by the ground-substance of the membrane, and bridged over by the flattened cells of the general

surface. In some folds of the serous membranes and especially in the great omentum of many animals, including man, the meshes of the reticulation have become open in many parts owing to the absorption of the intervening ground-substance and the perforation of the cells covering it, so as to allow of a free communication between the two sides of the fold of membrane. Where the membrane is thicker, the ground-substance contains blood-vessels and lymphatics, with the

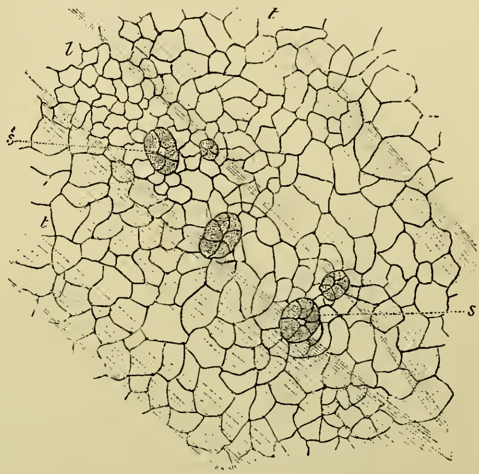


Fig. 449.—Small portion of peritoneal surface of diaphragm of rabbit. (Klein.) Magnified.

l, lymph-channel below the surface, lying between tendon bundles, *t*, *t*, and over which the surface-cells are seen to be relatively smaller, and to exhibit five stomata, *S*, *S*, leading into the lymphatic. The epithelium of the lymphatic channel is not represented.

lymphoid and adipose tissue which is so often found in the serous membranes and especially in their folds ; as well as connective tissue corpuscles with their corresponding cell-spaces (figs. 438, 439), which in the serous membranes are very often collected into endothelium-like patches. In parts of the membrane in which the corpuscles are more thinly scattered, they possess branching processes, some of which intercommunicate with those of neighbouring cells, others may pass up to the surface of the membrane as pseudostomata and others again become connected to the walls of the lymphatics and blood-vessels.

In the human subject, the serous membranes are bounded under the epithelium by a distinct basement membrane (Bizzozero).

The **blood-vessels** of the membrane end in a capillary network with comparatively wide meshes, which pervades the subserous tissue and the tissue of the serous membrane. The vessels are much more numerous in the nodules and tracts of lymphoid tissue (see below) as well as in the adipose tissue, which is found largely developed in the serous membranes of fat animals.

The **lymphatics** of the serous membranes are exceedingly abundant. Their relation both to the cell-spaces of the tissue and to the surface of the membrane, as well as their general arrangement, has been already noticed. They are sometimes met with ensheathing the blood-vessels.

Nodules of lymphoid tissue may occur, as before mentioned (p. 387), in the substance of the serous membranes. More generally the lymphoid tissue of the serous membranes takes the shape of elongated tracts which follow the course of the small arteries and veins, receiving from the latter branches which divide to form a capillary network. Lymphatic vessels run in these tracts alongside the blood-vessels, and often partially enclose them. These lymphoid nodules and tracts are more numerous in the young animal ; in the adult they are frequently found transformed into lobules and tracts of adipose tissue.

The **nerves** of the serous membranes are destined chiefly for the blood-vessels, and for the most part accompany these in their course. A few pale fibres, however, are distributed to the substance of the membrane, in which they form a plexus with large meshes : from the branches of this plexus, fibrils may be traced which unite into a somewhat finer plexus near the surface.

SYNOVIAL MEMBRANES.

These are connective tissue membranes which are found surrounding closed cavities in connection with moveable structures in certain parts, such as the joints, the elongated sheaths in which some tendons glide, and at various situations between the skin and bony prominences below it. Although they resemble serous membranes in some respects, the synovial membranes are distinguished by the nature of their secretion, which is a viscid glairy fluid resembling the white of an egg and named *synovia*. From its nature it is well adapted for diminishing friction, and thereby facilitating motion.

If a drop of synovial fluid is examined microscopically, it is found to contain (in addition to fat-molecules) a few amœboid corpuscles, as well as cells similar to those which occur on the projections of the membrane.

The different synovial membranes of the body are referred to three classes, viz., *articular*, *vaginal*, and *vesicular*.

1. Articular synovial membranes, or *Synovial capsules of joints*.—These by their secretion lubricate the cavities of the diarthrodial articulations, that is, those articulations in which the opposed surfaces glide on each other. In these cases the membrane may be readily seen covering internally the surface of the capsular and other ligaments which bound the cavity of the joint, and affording also an investment to any tendons or ligaments which pass through the articular cavity, as in the instance of the long tendon of the biceps muscle in the shoulder-joint. On approaching the articular cartilages the membrane does not pass over them, but terminates after advancing but a little way on their surface, with which it is here firmly adherent. The synovial membranes, therefore, do not form closed bags lying between the articular cartilages as was supposed by the older anatomists, for the main part of the surfaces of the joints is not covered at all by the membrane, nor even by a layer of epithelium-cells, prolonged from the membrane, as some have described.

In several of the joints, folds of the synovial membrane pass across the cavity ; these have been called synovial ligaments. Other processes of the membrane simply project into the cavity at various points. These are very generally cleft into fringes at their free border, upon which their blood-vessels, which are numerous, are densely distributed. The larger folds and processes often contain fat, and then are sufficiently obvious ; but many of the folds are small and inconspicuous.

The fringed vascular folds of the synovial membrane were described by Havers in 1691, under the name of the *mucilaginous glands*, and he regarded them as an apparatus for secreting synovia. Rainey found that these *Haversian fringes*, as they are sometimes called, may exist in all kinds of synovial membranes, and that from the primary vascular fringes other smaller secondary processes are sent off, into which no blood-vessels enter.

2. Vaginal synovial membranes, or *Synovial sheaths*.—These are intended to facilitate the motion of tendons as they glide in the fibrous sheaths which bind them down against the bones in various situations. The best-marked examples of such fibrous sheaths are to be seen in the hand and foot, and especially on the palmar aspect of the digital phalanges, where they confine the long tendons of the flexor muscles. In such instances one part of the synovial membrane forms a lining to the osseo-fibrous tube in which the tendon runs, and another part affords a close investment to the tendon. The space between these portions of the membrane is lubricated with synovia and crossed obliquely by one or more folds or duplications of the membrane named "fræna," in some parts inclosing a considerable amount of elastic tissue (J. Marshall).

3. Vesicular or **Bursal synovial membranes,** *Synovial bursæ, Bursæ mucosæ.*—In these the membrane has the form of a simple sac, interposed, so as to prevent friction, between two surfaces which move upon each other. The synovial sac in such cases is flattened and has its two opposite sides in apposition by their inner surface, which is free and lubricated with synovia, whilst the outer surface is attached by areolar tissue to the moving parts between which the sac is placed.

In regard to situation, the bursæ may be either deep-seated or subcutaneous. The former are for the most part placed between a muscle or its tendon and a bone or the exterior of a joint, less commonly between two muscles or tendons: certain of the bursæ situated in the neighbourhood of joints not unfrequently open into them. The subcutaneous bursæ lie immediately under the skin, and are found in various regions of the body interposed between the skin and some firm prominence

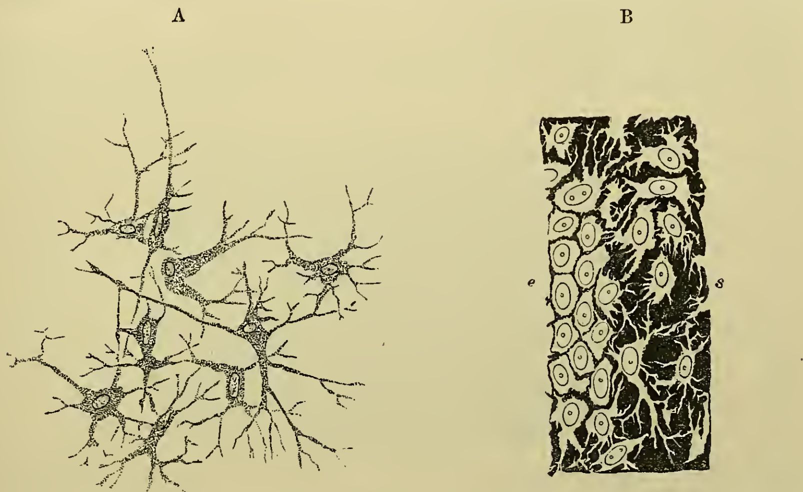


Fig. 450.—A. Ramified connective-tissue corpuscles, from articular synovial membrane of ox. Chloride of gold preparation. 250 diameters. (E. A. S.)

B. Portion of the surface of a vaginal synovial membrane, after treatment with nitrate of silver. 250 diameters. (E. A. S.)

The cell-spaces of the tissue and the nuclei of the contained cells only are represented. *e*, epithelioid arrangement of cells; *s*, ramified cells.

beneath it. The large bursa situated over the patella is a well-known example of this class, but similar though smaller bursæ are found also over the olecranon, the malleoli, the knuckles, and various other prominent parts. It must, however, be observed that, among these subcutaneous bursæ, some are reckoned which do not always present the characters of true synovial sacs, but look more like mere recesses in the subcutaneous areolar tissue, larger and more defined than the neighbouring areolæ, but still not bounded by an evident synovial membrane. These may be looked on as examples of less developed structure, forming a transition between the areolar tissue spaces and perfect synovial cavities; indeed it may happen that what is a well developed synovial bursa in one subject is merely an enlarged areola in another. Many of the bursæ do not appear until after birth, and they are said to increase in number as age advances.

Structure of synovial membranes.—The synovial membranes are composed entirely of connective tissue with the usual cells and fibres of that tissue. It was formerly stated, and is still asserted by some authors, that they are lined with an

epithelial layer of flattened cells, similar to those lining the serous membranes, but, as was shown by Hüter, there exists on the synovial membranes no complete lining of the kind. Patches of cells may, it is true, here and there be met with which present an epithelioid appearance (fig. 450, B, *e*), as, indeed, we know to be the case in the connective tissue of other parts; but most of the surface-cells of the synovial membranes are of the irregularly-branched type (fig. 450, A), the surface of the membrane between the cells and sometimes also over them being formed by the ground-substance of the connective tissue, whilst here and there small blood-vessels come close to the surface from subjacent parts. The cells are in many places smaller than in connective tissue generally. They vary much in shape in different parts, sometimes forming a network in the tissue by the anastomoses of their ramifying processes, in other parts being rounded, and more closely arranged.

The cells of the vaginal synovial membrane are often slightly elongated in the direction of the axis of the tendon.

The articular synovial membranes pass, as before said, a certain distance over the cartilages of the joints. They do not, however, end abruptly, but shade off gradually

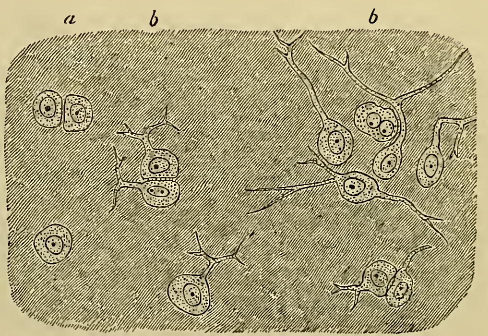


Fig. 451.—Transition of cartilage-cells into connective-tissue corpuscles of synovial membrane. About 340 diameters. From head of metatarsal bone, human. (E. A. S.)

a, ordinary cartilage cells ; *b*, *b*, with branched processes.

into the margin of the cartilage, the fibrous tissue becoming fibro-cartilage and the cells gradually losing their processes and becoming transformed into cartilage-cells (fig. 451), so that it is difficult to say where the one structure begins and the other ends. This portion of the synovial membrane, or of the cartilage, is known as the "marginal zone;" it is best marked around the convex heads of the bones, and is especially well seen near the lower margin of the patella (Hüter).

The Haversian folds and fringes, at least the larger ones, agree in general structure with the rest of the tissue of the synovial membrane, except that, as before remarked, some of them contain fat; their surface layer contains for the most part irregularly stellate cells, except over the fat, where there is occasionally to be observed a true epithelioid covering like that of a serous membrane. The smaller non-vascular secondary fringes of Rainey (*synovial villi*) are minute finger-shaped processes projecting from the margins of the larger ones, and consist for the most part of small rounded cells with granular protoplasm and but little intercellular substance, enclosing a central strand of connective-tissue fibrils; and in some cases a few cartilage-cells. Some of the synovial villi are entirely made up of fibro-cartilage, being altogether destitute of the covering of rounded cells (Tillmanns).

Vessels and lymphatics.—The blood-vessels in and immediately beneath the synovial membrane are numerous in most parts of the joints. They advance but a

short way upon the cartilages, forming around the margin a vascular zone, named by William Hunter "circulus articuli vasculosus," in which they end by loops of vessels dilated at the bent part greatly beyond the diameter of ordinary capillaries (Toynbee). In the fœtus these vessels advance further upon the surface of the cartilage than in the adult. The vessels of the vaginal synovial membranes are less numerous than those of the synovial membranes of the joints.

The synovial cavities do not appear to have so close a relation to the lymphatic system as is the case with the serous cavities. For although lymphatic vessels have been described by Tillmanns and others in the synovial membranes, they have not been shown to communicate with the cavities, nor do they as a rule lie near the free surface. In this respect they differ from the blood-capillaries, which may come close up to the inner surface of the membrane.

Nerves.—W. Krause described the nerves of the synovial membranes (at least those of the joints) as terminating in peculiar corpuscles allied to end-bulbs (p. 338 and fig. 398). Nicoladoni has traced nerves into a plexus of pale fibrils lying close under the surface of the membrane. Pacinian corpuscles have also been noticed under the synovial membranes in many places.

Development.—At the time of the formation of a joint by cleavage the tissue around it forms, in its outer part, the fibrous capsule of the joint ; in its inner part, the commencement of the synovial membrane. The cartilage cells on the surfaces of the newly formed joint are at first, like those of the embryonic cartilage generally, placed closely together without matrix or intercellular substance ; after a time this appears in fine lines between the cells, so that there is then presented, in silvered preparations, an epithelioid appearance. By a further development of intercellular substance the superficial cells become more separated from one another, and now possess an irregularly branched shape with communicating processes. Near the edge of the cartilage this condition is permanent, so that the marginal zone of the synovial membrane is formed *in situ* from what was originally cartilage. Nearer the centre of the articular surface, a further change takes place in the progress of development. The cells lose their processes and acquire the characters of ordinary cartilage-cells, whilst the matrix between them becomes increased, and forms also a thin layer covering their surface. In some places, *e.g.*, the glenoid cavity of the articulation of the lower jaw, the transformation into ordinary cartilage-cells may be incomplete, so that the synovial membrane extends over a larger extent of the articular surface than usual.

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SECRETING GLANDS.

The term gland has been applied to various objects, differing widely from each other in nature and office, but the organs the structure of which it is proposed to consider generally in the present chapter, are those devoted to the function of secretion.

The element which plays the most important part in the secretory process is the nucleated cell. A series of these cells, which are usually of a polyhedral or columnar figure, is spread over the secreting surface, in the form of an epithelium, which generally rests on a membrane, named the basement-membrane, or membrana propria. This membrane, itself extravascular, limits and defines the secreting surface ; it supports and connects the secreting cells on one side, whilst on the other it is bathed with lymph and is in close proximity to the blood-vessels. The basement-membrane when present is formed of flattened cells, which may be united edge to edge to form a complete limiting membrane, or may be branched and united by their processes with gaps between them (fig. 452). But a basement-membrane is not universally present, and it is the cells that are the chief agents in selecting and preparing the special ingredients of the secretions. They take into their interior those substances which, already existing in the blood, require merely to be segregated from the common store and concentrated in the secretion, and they, in certain cases, convert the matters which they have selected into new chemical compounds, or lead them to assume organic structure. A cell thus charged with its selected or converted contents yields them up to be poured out with the rest of the secretion—the contained substance escaping from it either by exudation or by bursting and destruction of the cell itself. Cells filled with secreted matter may also be detached, and carried out entire with the fluid part of the secretion; and, in all cases, new cells speedily take the place of those which have served their office. The fluid effused from the blood-vessels supplies matter for the nutrition of the secreting structure besides affording the materials of the secretion.

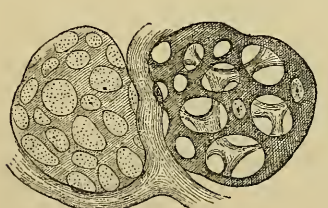

Fig. 452.—Membrana propria of two alveoli of the orbital gland of the dog. (Heidenhain and Lavdovsky.)

Changes in the cells during activity.—Since the materials for secretion are selected or prepared by the cells, it is not surprising to find that the cells of a secreting gland differ considerably in appearance according as the gland is in a condition of rest or activity (figs. 453, 454). In the former case the materials for secretion may have been accumulating within the cells and may be detected within them, whereas in the latter case, if the secretion have been proceeding for some time, the cells may be emptied of the accumulated material, and in many instances may themselves be partially or entirely destroyed, owing to the disruption of their protoplasm in the process of discharge of the secreted matter. In some glands however the accumulation of the materials of secretion within the cells does not go on to any great extent during rest, but begins with the increased activity of the gland consequent on stimulation whether natural or artificial, and proceeds up to a certain point, after which the process of discharge of the accumulated material begins. But according to Heidenhain and Langley the processes of growth of the protoplasm, formation of material for secretion, and discharge from the cell may all go on simultaneously, the material becoming formed by or from the cell protoplasm on the one hand, and discharged on the other hand into the commencement of the duct.

The material which accumulates within the cell is not always the same as that which appears in the discharged secretion. Thus in the glands which furnish the digestive ferments—especially the gastric glands and the pancreas—it has been

Fig. 453.—SECTIONS OF THE ORBITAL GLAND OF THE DOG. A, DURING REST. B, AFTER A PERIOD OF ACTIVITY. (Heidenhain and Lavdovsky.)

In A, the cells of the alveoli are large, being filled with the material for secretion (in this case, mucigen) which obscures their protoplasm, but some of the cells have not participated in the formation of the secretion, and these remain small and protoplasmic, forming the crescentic group seen in most of the alveoli.

In B, the accumulated material is discharged from the cells, which appear partially disintegrated in consequence. Both the cells and the alveoli are much smaller, and the protoplasm of all the cells is now apparent.

shown that the material which appears in the form of granules within the cells is not the pepsin and the trypsin which respectively characterise the secretions of those glands, but a precursor which is termed "zymogen," and is easily transformed into

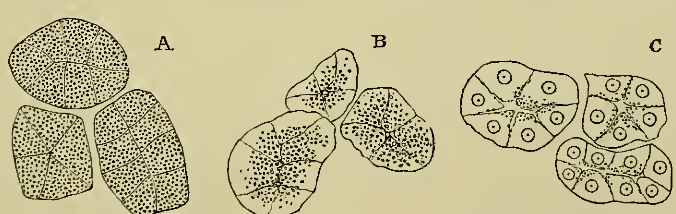

Fig. 454.—PART OF A FERMENT-FORMING GLAND; A AT REST, B AFTER A SHORT PERIOD OF ACTIVITY, C AFTER A PROLONGED PERIOD OF ACTIVITY. (Langley.)

In the resting condition the cells of the gland are almost filled with granules (of zymogen). During activity these become discharged from the cells as ferment, disappearing at first from the outer part of the cell, which is thereby left clear. Finally the granules only remain near the lumen of the alveoli, and near the surfaces of the cells which are contiguous to one another. In A and B the nuclei of the cells are obscured by the granules.

the ferments by the action of certain reagents; and it is supposed that a similar change may occur during the discharge of the secretion from the cells. Again, in the cells which secrete mucus, the substance which accumulates within the cells is not mucin, but a precursor of mucin, which is termed "mucigen," from the facility with which it becomes on discharge converted into mucin.

It is difficult to decide whether the material for secretion is formed by the direct conversion of a part of the protoplasm of the secreting cell, or from materials taken up from the plasma of the blood and elaborated by the agency of the protoplasm.

It is generally assumed that the former is the case, and that the protoplasm of the cells of a secreting gland increases in amount as the first stage in the process of formation of the secretion. But since the materials of secretion accumulate in the substance of the protoplasm, it may not be always possible to determine how much of the increase of size of the cell is due to a growth of the protoplasm itself, and how much to the accumulation of the materials of secretion, either entirely or only partially elaborated, within it.

The secretory changes which have been noticed by various observers in the cells of different glands, will be more fully described when the several glands are specially treated of.

Modifications in form of the secreting surface.—A secreting apparatus effectual for the purpose which it is destined to fulfil, may thus be said essentially to consist of a layer of secreting cells covering a free surface, whilst a layer of finely ramified blood vessels is generally spread out close to the attached ends of the cells, with sometimes a basement membrane between the two. But whilst the structure may remain essentially the same, the configuration of the secreting surface presents various modifications in different secreting organs. In some cases, the secreting

Fig. 455.—Plan of a secreting membrane. (Sharpey.)

a, membrana propria or basement-membrane; *b*, epithelium, composed of secreting cells; *c*, layer of capillary blood-vessels.

surface is plain, or, at least, expanded, as in various parts of the serous, synovial and mucous membranes, which may be looked on as examples of comparatively simple forms of secreting apparatus; but, in other instances, and particularly in the special secretory organs named glands, the surface of the secreting membrane is variously involved and complicated. An obvious effect of this complication is to increase the extent of the secreting surface in a secreting organ within a given bulk, and thus augment the quantity of secretion yielded by it. No connection has been clearly shown to exist between the *quality* of the secretion and the particular configuration, either internal or external, of the organ; on the other hand, we know that the same kind of secretion that is derived from a complex organ in one animal may be produced by an apparatus of most simple form in another.

There are two principal modes by which the surface of the membrane is so increased in extent, namely, by rising or protruding in form of a prominent fold or

Fig. 456.—Plan to show augmentation of surface by formation of processes. (Sharpey.)

a, *b*, *c*, as in preceding figure; *d*, simple and *e f*, branched or subdivided processes.

some otherwise shaped projection (fig. 456, *d*, *e*, *f*), or by retiring, in form of a recess (fig. 457, A, *g*, *h*).

The first-mentioned mode of increase, or that by *protrusion*, is not the one which is most generally followed in nature, still it is not without example, and, as instances, may be cited the Haversian fringes of the synovial membranes and the urinary organ of molluscs. In these cases, the membrane assumes the form of projecting folds, which, for the sake of further increase of surface, may be again plaited and complicated, or cleft and fringed, at their borders (fig. 456, *e*, *f*).

The augmentation of the secreting surface by *recession* or *inversion* of the membrane, in the form of a cavity, is, with few exceptions, that generally adopted in the construction of secreting glands. If the recess is simple its blind termination, which

is often enlarged, is spoken of as the "fundus" of the gland. If compound, its terminations are known as "alveoli." In a *simple gland* the shape of the cavity may be tubular (fig. 457, *g*) or saccular (*h*) : of these two kinds of simple gland the former is by far the more common. Examples of simple saccular glands are found in the skin of the frog (fig. 458) of simple tubular glands in the intestines (fig. 459). The secreting surface may be increased, in a simple tubular gland, by mere lengthening of the tube, in which case, however, when it acquires considerable length, the tube is coiled up into a ball (fig. 457, *i*), so as to take up less room, and adapt itself to receive compactly ramified blood-vessels. The sweat-glands of the skin are instances of simple glands formed of a long convoluted tube. But the chief means observed of further

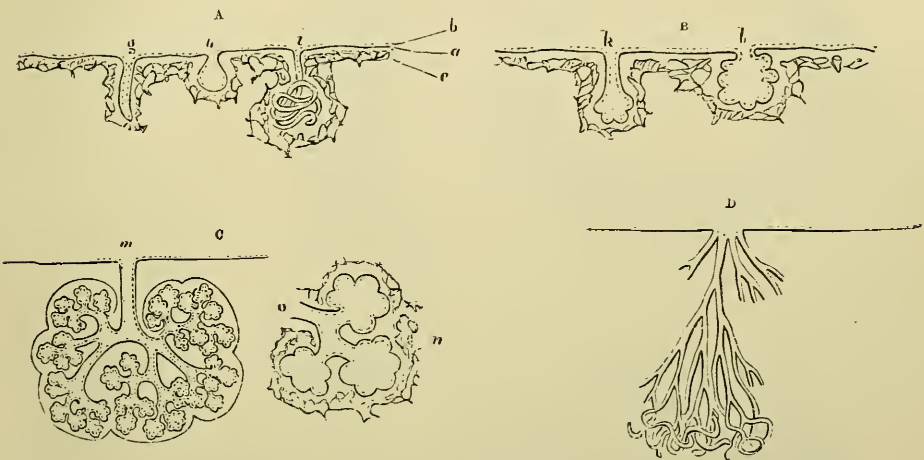

Fig. 457.—Plans of extension of secreting membrane, by inversion or recession. (Sharpey.)

A, simple glands, viz., *g*, straight tube ; *h*, sac ; *i*, coiled tube. B, simple glands with loculated walls ; *k*, of tubular form ; *l*, saccular. C, racemose, or acinous compound gland ; *m*, entire gland, showing branched duct and lobular structure ; *n*, a lobule, detached with *o*, branch of duct proceeding from it. D, compound tubular gland.

B and C represent rather the embryonic than the permanent condition of the acinous glands ; the actual condition of the alveoli in the adult condition being more like those shown in fig. 460.

increasing the secreting surface is by the subdivision, as well as extension, of the cavity, and when this occurs the gland is said to be *compound.* There is, however, a condition sometimes met with, in which the sides or extremity of a simple tube or sac merely become pouched or loculated (fig. 457, *k*, *l*), in which case the tube is termed the gland duct, or, as in Brunner's glands, and the small mucous glands generally, the pouchings or loculations may grow out into irregular tubular alveoli ; the gland is however still to be regarded as simple, since all the alveoli open into a single duct (Flemming).

In the compound glands, the divisions of the secreting cavity may assume a tubular or a saccular form, and this leads to the distinction of these glands into the "tubular," and the "acinous," or "racemose." The latter were so termed from the superficial resemblance which they bear, when examined with a lens, to a bunch of grapes. But it is found in most cases when their subdivisions are unravelled, that the apparent saccules are merely dilatations in the course of somewhat irregularly branching tubules (fig. 462); the glands are hence often named "acino-tubular.'

The disuse of the term racemose or acinous, as applied to these glands, has been advocated by Flemming on the ground that, as is well known, in many of these glands the terminal alveoli are not merely dilatations grouped around the endings of the ducts, but are distinctly

long and tubular in character; he proposes accordingly to group them along with such glands as the kidney and testicles as compound tubular glands. But since, as Chievitz has shown, the salivary and other similar glands, exhibit at an early condition of development a markedly sacculated character, the ultimate (tubular) alveoli being formed later as outgrowths of the saccules, whereas the tubular glands proper never exhibit this sacculated character, it appears desirable still to recognise a morphological difference between the two classes of glands.

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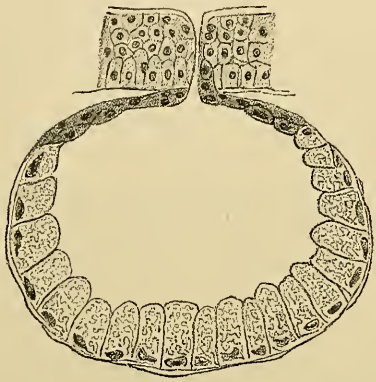

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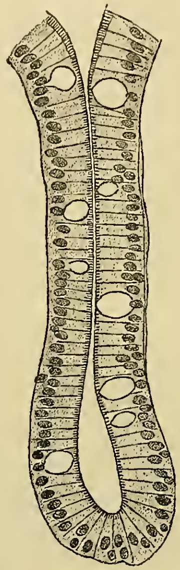

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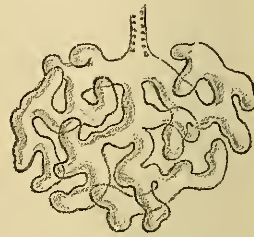

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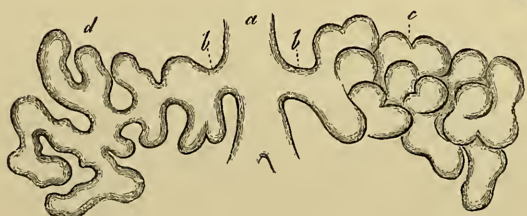

Fig. 458.—Simple saccular gland from the amphibian skin. (Flemming.)

Fig. 459.—Simple tubular gland from the human intestine. (Flemming.)

Fig. 460.—Diagram of small acinous gland formed of a simple "duct-system." (Flemming.)

461.—Part of a small "racemose" mucous gland of the tongue, showing the tubular character of the alveoli. (Flemming.)

Fig. 462.—Construction of a lobule of an "acinous" gland. (Kölliker.)

a, duct; *b.b*, branches of duct; *c*, alveoli as they lie together in the gland; *d*, the same unravelled, showing their connection as an irregular tube.

The **acinous, racemose** or **acino-tubular compound glands** (fig. 457, C) are composed of a multitude of alveoli, opening in clusters into the extremities of a branched tube, named the excretory duct. The alveoli are saccular, pyriform or tubular. They are often rather filled than lined by secreting cells; and are arranged in groups, round the commencing branches of the duct, with which their cavities are continuous (fig. 457, C). The ultimate branches of the duct open into larger branches (*o*), these into larger again, till they eventually terminate in one or more principal excretory ducts (*m*), by which the secretion is poured out of the gland. It is, as we have seen from the clustered arrangement of their ultimate recesses, that these glands are named "racemose" or grape-like; and they, for the most part, have a dis-

tinctly lobular structure. The lobules are held together by the branches of the duct to which they are appended, and by interlobular connective tissue which also supports the blood-vessels in their ramifications. The larger lobules are made up of smaller ones, these of still smaller, and so on for several successive stages. The smallest lobules consist of a single group of alveoli, collected around a small duct, which issues from the lobule. This issuing duct is often markedly narrower than either the alveoli or the larger duct into which it opens, but since it is lined by somewhat flattened epithelium its lumen is quite as large as that of the alveoli (fig. 463, *d'*) ; and a collection of the smallest lobules, united by connective tissue and vessels, forms a lobule of the next size, which, too, has its larger branch of the duct formed by the junction of the ramuli belonging to the ultimate lobules. In this way the whole gland is made up, the number of its lobules and of the branches of its duct depending on its size ; for whilst some glands of this kind, like the parotid, consists of innumerable lobules, connected by a large and many-branched duct, others, such as some of the sebaceous glands of the skin, are formed of but two or three ultimate lobules, or even of a single one. In fact, a small racemose gland resembles a fragment of a larger one.

The smallest lobules were originally called *acini*, a term which is now often used to denote the alveoli.

The alveoli are lined, and sometimes almost filled by the secreting cells, a cavity being left in the centre communicating with the excretory duct (fig. 463). In some

Fig. 463.—Section of a racemose gland, showing the commencement of a duct in the alveoli. Magnified 425 diameters. (E. A. S.).

a, one of the alveoli, several of which are in the section shown grouped around the commencement of the duct, *d'*; *a'*, an alveolus, not opened by the section ; *b*, basement-membrane in section ; *c*, interstitial connective tissue of the gland ; *d*, section of a duct which has passed away from its alveoli, and is now lined with characteristically-striated columnar cells; *s*, semilunar group of darkly-stained cells at the periphery of an alveolus.

glands karyomitotic figures are numerous in the cells, indicating rapid cell-multiplication, whereas in others such indication is lacking (Gaule, Bizzozero). In some cases, minute canals have been described as leading from the central cavity between the cells, and these may aid in the conveyance of the secretion of the latter into the cavity. Further the flattened cells which compose the basement-membrane may send delicate lamellar processes between the alveolar cells, among which they form a sustentacular network (Boll, Ebner).

Many glands, yielding very different secretions, belong to the racemose class. As examples, it will be sufficient to mention the salivary, lacrymal, and mammary glands.

Of the **tubular compound glands**, the most characteristic examples are the testicle and kidney. In these the tubular ducts divide again and again into branches, which, retaining their tubular form, are greatly lengthened out. The branches of the ducts are formed, as usual, of a limitary or basement-membrane (*membrana*

propria), lined by epithelium. By the multiplication and elongation of the tubular branches, a vast extent of secreting surface is obtained, the tubes being partly coiled up into a compact mass, which is traversed and held together by blood-vessels, and sometimes also divided into lobules and supported, as in the testis, by fibrous partitions, derived from the inclosing capsule of the gland. In consequence of their intricately involved arrangement, it is sometimes difficult to find out how the tubular ducts are disposed at their extremities. In the testis some are free, and simply closed without dilatation, and others anastomose with neighbouring tubes, joining with them in the form of loops ; in the kidney, little round tufts of fine blood-vessels project into terminal dilatations of the ducts, but without piercing the basement membrane.

Certain glands do not precisely agree in structure with either of the above classes of compound glands. One of these is the adult mammalian liver. Its secreting cells are collected into small polyhedral masses termed the hepatic lobules, pervaded by a network of capillary blood-vessels ; and the ducts begin within the lobules, in the form of a network of fine channels which run between the sides of contiguous cells. At an early stage of development the liver has, however, a distinctly tubular character, a condition which is permanent in most of the lower vertebrata. Another is the ovary, the alveoli of which are isolated and unprovided with ducts. They are known as the Graafian follicles. When distended by secretion they burst, and the secretion escapes, carrying the ovum along with it. They are originally developed as tubules filled with epithelium (" egg-tubes " of Pflüger).

The thyroid gland is another body which in the adult consists of isolated vesicles, but in the embryo has the form of a ramified tubular gland. The same remark applies to the anterior lobe of the pituitary body.

Besides blood-vessels, the glands are furnished with lymphatics, which in most compound glands proceed from interstitial lymphatic spaces which surround the alveoli. Branches of nerves have also been followed for some way into these organs; and that an influence is exerted on secreting organs through the medium of the nervous system, is shown by the fact, that the flow of secretion in several glands is affected by mental emotions, and that the flow of secretion from many glands may be brought on by direct or reflex stimulation of their nerves. In some cases also an increased accumulation of the materials of secretion within the cells, may thus be produced. Fine non-medullated nerve-fibres have in several instances been described as entering between the cells of the alveoli ; and in the salivary glands, Pflüger has affirmed a direct passage of nerve-fibres, both medullated and non-medullated, into the secreting cells. His observations, however, have not been confirmed by other inquirers, although Kupffer has described a similar connection between nerve-fibres and secreting cells in the salivary glands of insects.

Uniting the several parts of a compound gland is a certain amount of interstitial connective tissue, which varies in character in different glands, being in some more fibrous, in others more cellular, and in others again being represented by retiform tissue.

Some glands have a special envelope, as in the case of the kidney and testis.

The ducts of glands ultimately open into cavities lined by mucous membrane, or upon the surface of the skin. They are sometimes provided with a reservoir, in which the secretion is collected, to be discharged at intervals. The reservoir of the urine receives the whole of the secreted fluid ; in the gall-bladder, on the other hand, only a part of the bile is collected. The vesiculæ seminales afford another example of these appended reservoirs. The ducts are constructed of a basement-membrane and lining of epithelium, and in their smaller divisions there is nothing more ; but in the larger branches and trunks, a coat, composed of connective tissue,

with which in some cases involuntary muscular fibres, running circularly, are introduced, is added. In the sweat glands, the muscular fibres run longitudinally, and lie between the basement-membrane and the epithelium of the tubular alveoli. The epithelium-cells are usually flattened at the commencement of the duct, where these emerge from the alveoli, and are columnar in the rest of the duct. In some glands the columnar cells of the ducts exhibit a peculiar striated appearance (fig. 463, *d*) in the part of the cell next to the basement-membrane, and the alveolar cells may also exhibit a similar appearance, but far less distinctly.

Mechanism of the discharge of secretion from a gland.—Although no doubt dependent ultimately upon physical and chemical conditions, it is not known precisely in what way the discharge of secretion from the gland-cells, and eventually from the gland, is effected. The forces which produce the discharge are, however, considerable, and are influenced as we have seen through the nervous system. In the cutaneous glands of the frog, Stricker and Spina have noticed that irritation of the nerves is followed by swelling and enlargement of the previously flattened cells of the gland, and that this enlargement causes a discharge of secretion from the mouth of the duct. The swelling is produced by an accumulation of fluid, derived from the plasma of the blood, within the cells, and when these come again to the condition of rest and resume the flattened form, the fluid is supposed to pass from them into the cavity of the alveolus, carrying with it the materials of secretion extracted from the cells. If the glands are again stimulated the same process is gone through, and in this way it is supposed an intermittent discharge may be caused. There is no evidence, however, to show that similar changes occur in other glands, nor is it explained how it happens that the water of the plasma should pass into the cells only under the influence of excitation.

The observations of v. Gehuchten seem to point to the *vis-a-tergo* of the accumulating secretion as the main agent in effecting the discharge of the secretion from the cells. The discharge from the ducts of a gland is no doubt partly due to the *vis-a-tergo* of the accumulating secretion, partly to the peristaltic contraction of the muscular tissue in the wall of the duct (where this tissue exists).

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MUCOUS MEMBRANES.

These membranes, unlike the serous, line passages and cavities which communicate with the exterior, as well as recesses, ducts and receptacles of secretion, which open into such passages. They are habitually subject either to the contact of foreign substances introduced into the body, such as air and aliment, or of various secreted or excreted matters, and hence their surface is coated over and protected by mucus, a fluid of a more consistent and tenacious character than that which moistens the serous membranes.

The mucous membranes of several different or even distant parts are continuous, and they may all, or nearly all, be reduced to two great divisions, namely, the *gastro-pneumonic* and *genito-urinary*. The former covers the inside of the alimentary and air-passages as well as the less considerable cavities communicating with them. It may be described as commencing at the edges of the lips and nostrils, where it is continuous with the skin, and proceeding through the nose and mouth to the throat, whence it is continued throughout the whole length of the alimentary canal to the termination of the intestine, there again meeting the skin, and also along the wind-pipe and its numerous divisions as far as the air-cells of the lungs, to which it affords a lining. From the nose the membrane may be said to be prolonged into the lachrymal passages, extending up the nasal duct into the lachrymal sac and along the lachrymal canals until, under the name of the conjunctival membrane, it spreads over the fore part of the eyeball and inside of the eyelids, on the edges of which it meets with the skin. Other offsets from the nasal part of the membrane line the frontal, ethmoidal, sphenoidal and maxillary sinuses, and from the upper part of the pharynx a prolongation extends on each side along the Eustachian tube to line that passage and the tympanum of the ear. Besides these there are offsets from the alimentary membrane to line the salivary, pancreatic, and biliary ducts, and the gall-bladder. The *genito-urinary* membrane invests the inside of the urinary bladder and the whole tract of the urine in both sexes, from the interior of the kidneys to the orifice of the urethra, also the seminal ducts and vesicles in the male, and the vagina, uterus and Fallopian tubes in the female.

By one surface the mucous membranes are attached to the parts which they line or cover, by means of areolar tissue, named "submucous," which differs greatly in quantity as well as in consistency in different parts. The connection is in some cases close and firm, as in the cavity of the nose and its adjoining sinuses ; in other instances, especially in cavities subject to frequent variation in capacity, like the gullet and stomach, it is lax and allows some degree of shifting of the connected surfaces. In such cases as the last-mentioned, the mucous membrane is accordingly thrown into folds when the cavity is narrowed by contraction of the exterior coats of the organ, and of course these folds, or *rugæ* as they are named, are effaced by distension. But in certain parts the mucous membrane forms permanent folds, not capable of being thus effaced, which project conspicuously into the cavity which it lines. The best-marked example of these is presented by the *valvulæ conniventes* seen in the small intestine. These, as is more fully described in the special anatomy of the intestines, are crescent-shaped duplicatures of the membrane, with connecting areolar tissue between their laminæ, which are placed transversely and follow one another at very short intervals along a great part of the intestinal tract. The chief use of the valvulæ conniventes is doubtless to increase the surface of the absorbing mucous membrane within the cavity.

In most situations the mucous membranes are nearly opaque or only slightly translucent. They possess no great degree of tenacity and but little elasticity, and

hence are readily torn by a moderate force. The redness which they commonly exhibit during life, and retain in greater or less degree in various parts after death, is due to the blood contained in their vessels. The degree of redness is greater in the fœtus and infant than in the adult. It is greater too in certain situations ; thus, of the different parts of the alimentary canal, it is most marked in the stomach, pharynx, and rectum.

Structure.—A mucous membrane is composed of *corium* and *epithelium.* The *epithelium* covers the surface. The membrane which remains after its removal is named the *corium,* as in the analogous instance of the true skin.

The **epithelium** is the most constant part of a mucous membrane, being continued over certain parts to which the other constituents of the membrane cannot be traced, as over the alveoli of the lungs, and the front of the cornea of the eye. It may be scaly and stratified as in the mouth and throat, columnar as in the intestine, or ciliated as in the respiratory tract and uterus. When a mucous membrane is covered with an epithelium of the scaly and stratified variety, the mucus which moistens its surface is derived from glands in the membrane, which are lined with columnar and polyhedral secreting cells ; but when a columnar epithelium or a ciliated epithelium covers the surface, a large part of the mucus is formed in the cells of this layer, and the glands of the membrane are frequently devoted to the elaboration of some special secretion. The secretion is not as a rule formed at the same time in all the cells of the epithelium, but in some only. The first appearance of the mucigen within the cell is in the form of granules ; these appear to become enlarged, and eventually, as they are becoming transformed into mucus, they form clear swollen masses filling a large part of the cell, especially near its free border (fig. 464, m^1, m^2, m^3).

A

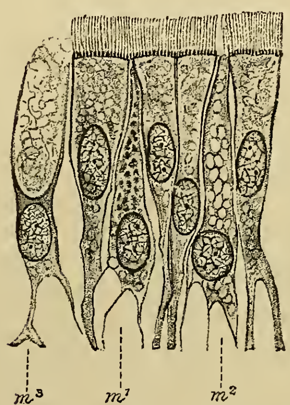


Fig. 464.—A. Columnar epithelium from the mucous membrane of the trachea. (E. A. S.)

m^1, m^2, m^3, mucus-secreting cells between the ciliated cells, showing three stages in the formation of the secretion.

B

B.—A mucus-secreting cell from the trachea ; more highly magnified.

Those cells which are concerned in the production of mucus often become greatly distended with the accumulated mucigen into the shape of a goblet or chalice, and this may in many be seen to have become exuded from the free and apparently open end of the cell as a droplet of mucus. A certain number of these *goblet-* or *chalice-cells* are almost always to be found in columnar epithelium covering mucous membranes. It is somewhat uncertain whether after discharge of their secretion they become reconverted into ordinary epithelium-cells, or whether they permanently maintain the chalice-like form, their cavity becoming again filled with secretion during rest. If the latter is the case the cells in question are analogous to the uni-cellular glands which are met with in the integument of some of the invertebrate animals.

The **corium** of a mucous membrane consists of connective tissue, either areolar

or retiform tissue. It is usually bounded next to the epithelium by a basement membrane (fig. 465, *bm*), and next to the submucous tissue by a thin layer of non-striated muscular tissue termed the *muscularis mucosæ* (*mm*).

The *basement membrane* is not everywhere demonstrable, but where it is well marked it appears in section as a thin line immediately underlying the epithelium. Viewed on the flat and with the superjacent epithelium removed, the membrane in question seems at first sight homogeneous; but treatment with nitrate of silver brings to view the outlines of the flattened cells of which it is in reality composed.

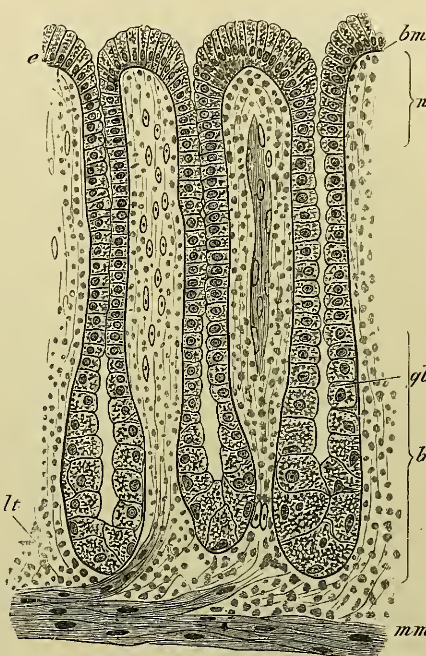


Fig. 465.—Section of mucous membrane from the stomach of the kangaroo. Magnified about 260 diameters. (E. A. S.)

e, columnar epithelium of the surface, continued into the neck, *n*, of the simple tubular glands, *gl*; but becoming at first cubical, and then polyhedral towards the base, *b*, of the glands; *lt*, lymphoid tissue; *bm*, basement membrane, bounding the corium superficially; *mm*, muscularis mucosæ, bounding the mucous membrane at its attached surface, and sending small bundles of plain muscular tissue between the glands. The commencement of a lymphatic vessel is shown between two of the glands.

It is not always a complete membrane, for in some parts the cells composing it, instead of adhering closely by their edges, intercommunicate by branching processes so as to form a network instead of a continuous membrane. The basement membrane follows all the eminences and depressions of the surface of the mucous membrane, dipping down to take part in the formation of the wall of the glands, and passing over the raised villi and other prominences.

The *muscularis mucosæ* forms the deepest part of a mucous membrane, but it is not everywhere present. It is best developed in the mucous membrane of the alimentary canal, in some parts of which it may consist of two layers, in the one of which the fibres are longitudinal, in the other circular in direction. From its inner surface muscular bundles bend inwards into the thickness of the mucous membrane, passing between the glands contained within it, and even into its prominences, so as in many cases to reach and become attached to the basement-membrane covering them (as in the villi of the small intestine). The muscularis mucosæ is a part therefore of the mucous membrane, and is not to be confounded with the muscular coat proper, which forms a separate layer in most of the hollow viscera.

The *connective tissue layer* or *corium proper* varies much in structure in different parts. In some situations, as in the gullet, bladder, and vagina, the filamentous connective tissue is abundant, and extends throughout its whole thickness, forming a continuous and tolerably compact web, and rendering the mucous membrane of those parts comparatively stout and tough. In the stomach and intestines, on the other hand, where the membrane is pervaded by tubular glands, the tissue between these is chiefly retiform or lymphoid tissue (fig. 465, *lt*) with but few white and elastic fibres, and hence in these situations the membrane, although thicker, is far less firm and tough than in parts where much of the white connective tissue is

found. In other mucous membranes transitions are met with between these two extremes.

It frequently happens that in certain circumscribed places the lymphoid tissue is greatly increased in amount, and becomes densely packed with lymphoid cells. In this way the so-called *solitary glands, lymphoid follicles* or *lymphoid nodules* are produced. If there are many lymphoid nodules adjacent to one another, so as to make up a localized patch, a so-called *agminated gland* is formed, or if massed together more thickly, a lymphoid organ like the *tonsil.* These collections of lymphoid tissue, which may if large extend, on the one hand, down into the submucous tissue, and on the other, upwards into the epithelium, have been already referred to (p. 388), and will be more particularly described when the several parts in which they occur come under consideration. The lymph-cells of this tissue migrate between the cells of the epithelium which covers the surface, and may even become free in considerable numbers in the fluid which moistens the surface (Stöhr). The purpose served by this emigration of lymph-cells is not understood.

Blood-vessels are abundant in most mucous membranes. The branches of the arteries and veins, dividing in the submucous tissue, send smaller branches into the corium, which divide to form a network of capillaries in the latter. This capillary network lies immediately beneath the epithelium, or the basement-membrane when this is present, advancing into the villi and papillæ to be presently described, and surrounding the tubes and other glandular recesses. The **lymphatics** also form networks of cleft-like vessels in the mucous membrane, which communicate with plexuses of larger valved vessels in the submucous tissue; they commence either by blind diverticula, as in the villi, or in the form of a superficial network, which is almost always more deeply placed than the network of blood-capillaries. The lymphatic vessels often form sinus-like dilatations around the bases of the lymphoid nodules.

The **nerves** of mucous membranes seem chiefly to be distributed to the muscularis mucosæ where this exists. Before proceeding to their destination they are in many parts collected together to form a gangliated plexus in the submucous tissue, such as the plexus of Meissner in the alimentary canal. Some nerves pass however to the epithelium and terminate between the epithelial cells; at least this has been shown to be the case in the stratified epithelium which covers the mucous membranes of certain parts.

Papillæ and villi.—The free surface of the mucous membranes is in some parts plain, but in others is beset with little eminences named papillæ and villi. The *papillæ* are best seen on the tongue; they are small processes of the corium, mostly of a conical or cylindrical figure, containing blood-vessels and nerves, and covered with epithelium. Some are small and simple, others larger and covered with secondary papillæ. They serve various purposes; some of them no doubt minister to the senses of taste and touch, many appear to have chiefly a mechanical office, while others would seem to give greater extension to the surface of the corium for the production of a thick coating of epithelium. The *villi* are most fully developed on the mucous coat of the small intestines. Being set close together like the pile of velvet, they give to the parts of the membrane which they cover the aspect usually denominated "villous." They are in reality little elevations or processes of the corium, covered with epithelium, and containing blood-vessels and lacteals, which are thus favourably disposed for absorbing nutrient matters from the intestine. The more detailed description of the papillæ and villi belongs to the special anatomy of the parts in which they occur.

In some few portions of the mucous membranes the surface is marked with fine ridges which intersect each other in a reticular manner, and thus inclose larger and smaller polygonal pits or recesses. This peculiar character of the surface of the membrane, which has been termed "alveolar," is seen very distinctly in the gall-

bladder, and on a finer scale in the vesiculæ seminales; still more minute alveolar recesses with intervening ridges may be discovered with a lens on the mucous membrane of the stomach.

Glands of mucous membranes.—Many, indeed most, of the glands of the body pour their secretions into the great passages lined by mucous membranes; but there are certain small secreting glands which may be said to belong to the membrane itself, inasmuch as they are found in numbers over large tracts of that membrane, and yield mucus or special secretions known to be formed in particular portions of the membrane. Omitting local peculiarities the glands referred to may be described as of two kinds, viz. :—

I. *Simple tubular glands* (*crypts*).—These are minute tubes formed by recesses or inversions of the basement membrane, and lined with epithelium (fig. 465, *gl*). They are usually placed perpendicularly to the surface and often very closely together, and they constitute the chief substance of the mucous membrane in those parts where they abound, its thickness depending on the length of the tubes, which differs considerably in different regions. The tubes open by one end on the surface; the other end is closed, and is either simple or cleft into two or more branches. Such tubular glands are abundant in the stomach, and in the small and large intestines, where they are comparatively short and known as the crypts of Lieberkühn. They exist also in considerable numbers in the mucous membrane of the uterus, when they are longer and tend to be convoluted.

II. *Small racemose glands.*—Under this head are here comprehended minute glands of the racemose or acino-tubular kind, which open on the surface of the membrane by a longer or shorter duct. Numbers of these, yielding some a mucous, others a more albuminous or watery secretion, open into the mouth. To the naked eye they have the appearance of small solid bodies, often of a flattened lenticular form, but varying much both in shape and size, and placed at different depths below the mucous membrane on which their ducts open. They are also met with throughout the pharynx and gullet and in the larynx, trachea, and bronchial tubes, but in all these parts their secretion is purely of a mucous character. The glands of Brunner, which are met with in the submucous tissue of the duodenum, near its junction with the stomach, also bear a superficial resemblance to the racemose mucous glands, and in minute structure they are not unlike them, but the nature of their secretion appears to be different.

The several mucous membranes are described more in detail when the organs of which they form a part are treated of, and the works which refer to them may then also be mentioned most appropriately.

THE SKIN.

The skin consists of the cutis vera or corium, and the cuticle or epidermis.

The **epidermis, cuticle, or scarf-skin,** belongs to the class of stratified epithelia, the general nature of which has been already considered. It forms a protective covering over every part of the true skin. The thickness of the cuticle varies in different parts of the surface, measuring in some places not more than $\frac{1}{240}$th, and

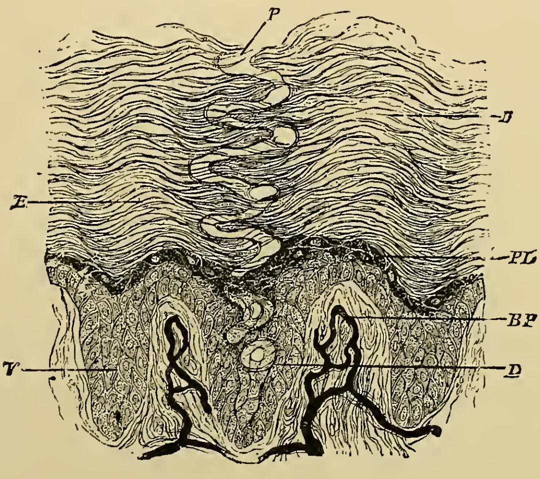


Fig. 466.—Section of human epidermis with two vascular papillæ of the corium. (Heitzmann.)

B.P, loop of capillary vessels in papilla ; *V*, rete mucosum ; *P.L*, stratum granulosum ; *E*, stratum corneum ; *D to p*, duct of sweat-gland passing through the epidermis.

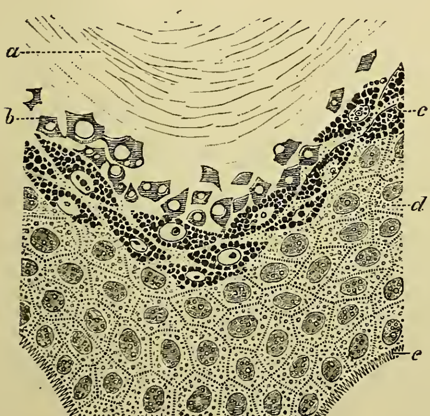
in other parts, as much as $\frac{1}{24}$th of an inch (about a millimeter), or even more than this in some individuals. It is thickest in the palms of the hands and soles of the feet, where the skin is much exposed to intermittent pressure, and it is not improbable that such pressure may serve to stimulate the adjacent true skin to a more active formation of epidermis ; but the difference does not depend immediately on external causes, for it is well marked even in the fœtus.

The more firm and transparent superficial part, or horny layer, of the epidermis, may be separated after maceration from the deeper, softer, more opaque, and recently formed part, which constitutes what is called the Malpighian layer, or *rete mucosum.*

The under or attached surface of the cuticle is moulded on the adjoining surface of the corium, and, when separated by maceration or putrefaction, presents impressions corresponding exactly with the papillary or other eminences, and the furrows or depressions of the true skin ; the more prominent inequalities of the latter are marked also on the outer surface of the cuticle, but less accurately. Fine tubular prolongations of the cuticle sink down into the ducts of the sweat-glands, and are often partially drawn out from their recesses when the cuticle is detached, appearing then like threads proceeding from its under surface.

Structure.—The cuticle is made up of cells agglutinated together in many irregular layers. The deepest cells are elongated in figure, and placed perpendicularly on the surface of the corium (fig. 467, *e*) ; they are denticulate at their lower ends, and fit into corresponding fine denticulations of the corium. The perpendicular cells generally form one stratum ; above them are cells of a more rounded or polyhedral shape (*d*). The cells have fine intercellular clefts or channels between them, bridged across by fibres which pass from cell to cell, as in all stratified epithelia (see p. 196). These so-called "spiny cells" form several strata ; above, they become gradually more flattened, conformably to the surface, until a layer, often incomplete, is reached in which the cells have a markedly granular appearance (Langerhans). This has been termed the *stratum granulosum.* The granules in the cells are composed of a peculiar matter (*eleidin* of Ranvier, *keratohyalin* of

Waldeyer), staining deeply with carmine, and they are thought by some to have an intimate relation to the formation of the horny substance in the more superficial cells. Immediately above the stratum granulosum is a clear-looking layer in which the outlines of the cells are somewhat indistinct, owing to the fact that they have undergone a transformation into horny material. This layer, which is not always sharply marked off from the one superficial to it, has been termed *stratum lucidum*, and may be looked upon as the commencement of the horny layer of the epidermis. Superficial to it is a stratum which in some parts is of considerable thickness, and in which the cells are much enlarged, and the nuclei in many cases no longer visible (*a*) : still nearer the surface this passes into a stratum of hard flattened scales which are being thrown off by desquamation. As the cells change their form, they undergo chemical and physical changes in the nature of their contents ; for in the rete mucosum they consist of a soft, granular, protoplasmic matter, whilst the superficial ones are transparent, dry, and horny. These dry hard



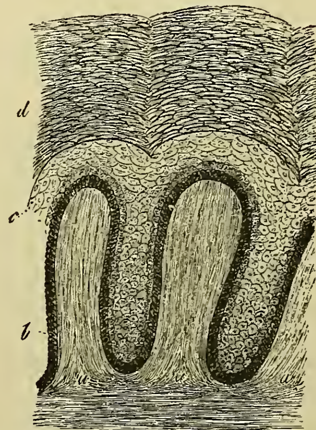


Fig. 467.—Section of epidermis from the skin of the finger, coloured by picrocarmine. (Ranvier.)

a, stratum corneum ; *b*, stratum lucidum, some of the cells of which are filled with flakes of eleidin ; *c*, stratum granulosum, full of eleidin granules or drops ; *d*, spring and fibrous cells of rete mucosum ; *e*, dentations of deepest cells, for attachment to cutis vera.

Fig. 468.—Skin of the negro, vertical section, magnified 250 diameters. (Kölliker.)

a, *a*, cutaneous papillæ ; *b*, undermost and dark-coloured layer of oblong vertical epidermis-cells ; *c*, mucous or Malpighian layer ; *d*, horny layer.

scales may be made to reassume their cellular form, by exposure for a few minutes to a solution of caustic potash or soda, and then to water. Under this treatment they are softened by the alkali, and distended by imbibition of water.

As Zander has pointed out, there are two types of horny layers in the epidermis. The epidermis which covers the greater part of the surface of the body has a horny layer which is composed exclusively of thin flattened scales, whereas that which covers those parts of the skin which have a thicker epidermis and are not provided with hairs, is mainly composed of large swollen-out cells, with a central cavity. These cells perhaps represent the epitrichial layer which during a certain period of fœtal development covers the whole surface of the body, but is thrown off elsewhere as the hairs become developed (see next page).

Many of the cells of the cuticle contain pigment-granules, and in parts give the membrane more or less of a tawny colour, even in the white races of mankind ; the blackness of the skin in the negro depends entirely on the cuticle. The pigment is

contained principally in the cells of the deep layer or the rete mucosum (fig. 468), but even the superficial part possesses a certain degree of colour.

In the intercellular channels of the Malpighian layer lymph-corpuscles, rounded or branched, are occasionally observed, and these, in the negro, may also contain pigment-granules. It has been supposed that these cells may act as carriers of pigment to the epidermis, since leucocytes containing pigment are also found in the negro in the superficial layers of the cutis vera. This is also the case in the bronzed skin of Addison's disease.

Development of the Epidermis.—The epidermis is derived from the cutaneous epiblast. Up to about the second month of intra-uterine life it consists, according to Kölliker, of two layers of protoplasmic cells, of which the deeper are smaller and rounded, the more superficial larger and polygonal. The latter multiply, and in the second month are two or three cells deep; they are clearer and more flattened out than the deep layer of cells, and stain less deeply with carmine.

Fig. 469.—Section of epidermis from the occiput of a fœtus of 2½ months. (Bowen.)

Fig. 470.—Section of epidermis from the palm of a 3 months fœtus. (Bowen.)

ep, epitrichial layer.

Between the second and third month there is found, according to the observations of Minot and Bowen, forming the most superficial layer of the epidermis, a stratum of enlarged, swollen-out cells (fig. 469). These were first noticed by Zander upon the fingers and toes of embryoes of about thirteen weeks or more, and were termed by him "bladder" cells. The layer increases for a time in thickness, so as to be two or three cells deep (fig. 470), or even in certain parts, *e.g.*, over the situation of the developing nails and on the palmar surface of the hand and feet, to acquire a considerable thickness. Here the stratum seems to persist, but it disappears over the body of the nail, and also over the remainder of the surface of the skin, so that by the sixth month it is only found near the free border and root of the nail, and perhaps forming the thick horny layer of the palms and soles, which belongs to the second type of horny layer of Zander. This layer of bladder-like cells appears to correspond with an epithelial membrane which was first noticed by Welcker in a sloth-embryo, covering the surface of the body and lying over the developing hairs, hence named by him *epitrichium*. It has accordingly been termed the *epitrichial layer*, and has been shown to be of wide occurrence in the embryoes of mammals and birds, and also to be represented in reptiles.

The cells of the fœtal epidermis underneath this epitrichial layer form the Malpighian layer, and eventually the more superficial develop granules of eleidin and become keratinized, so that a stratum corneum is produced. After the throwing off of the epitrichial layer, the superficial cells of the stratum corneum also become gradually cast off, whilst others pass from the Malpighian layer to replace them. The cast-off scales, mingled with secretion of the cutaneous glands, form it with a yellowish caseous layer covering the surface of the fœtus (smegma embryonum, vernix caseosa), and occurring also in flakes in the amniotic fluid.

The pigmentation of the Malpighian layer in the coloured races of mankind frequently does not appear until a day or two after birth; probably because it is concealed by the moist and therefore opaque epidermis over it. In the negro the pigment is certainly present even some weeks before term.

The growth of epidermis continues throughout life. The cells of the Malpighian layer are constantly undergoing multiplication, and the new cells thus produced push outwards those which are previously formed. The more superficial cells of the Malpighian layer are thus continually passing on to reinforce the horny layer, the cells as they proceed outwards becoming flattened and transformed into horny matter. This change seems to occur quite abruptly when the stratum lucidum is reached; beyond this the cells again swell out somewhat, until on reaching the most superficial layers they are entirely transformed into structureless horny scales which are constantly undergoing desquamation. The cells of the stratum lucidum sometimes contain drops of a semi-fluid substance which stains similarly to the eleidin of the stratum granulosum (fig. 467, *b*). It has accordingly been inferred that the horny substance of these cells and therefore of the whole horny layer of the epidermis is due to a chemical transformation of the eleidin which is formed in the most superficial layer of the rete mucosum. But a genetic relation between eleidin and keratin is rendered improbable if the statement which has been made by some authors is correct, that in some parts of the epidermis where a large amount of keratin is produced, eleidin granules are not formed within the cells of the rete mucosum.

There is reason to suppose that the regeneration of epidermis, when a portion has been removed by a blister or wound of any kind, takes place, like its growth, only from cells of the Malpighian layer. If the whole of the epidermis has been destroyed or removed over an extensive surface, the process of regeneration is very slow, since the new covering has to grow in from the epidermis at the margins of the wound. But if the deeper cells have not been wholly removed the regeneration may start from the places where any of them still remain, and the formation of the new covering is proportionately quicker. In the operation of skin-grafting so-called, the surgeon endeavours to transplant from a healthy portion of skin small pieces of the epidermis, including its deeper layers, to the denuded surface: if the operation succeed, each such graft acts as a centre from which the new formation of epidermis may spread, and in this way the raw surface may be much more speedily covered.

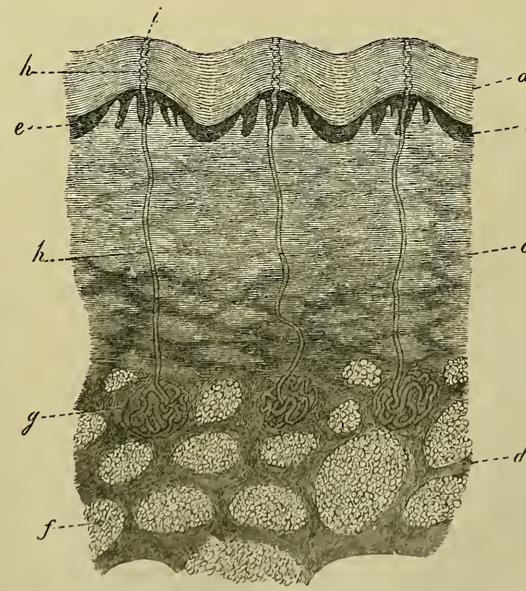


Fig. 471.—Vertical section of the skin and subcutaneous tissue, from the end of the thumb, across the ridges and furrows. Magnified 20 diameters. (Kölliker.)

a, horny, and *b*, Malpighian layer of the epidermis; *c*, corium; *d*, *panniculus adiposus*; *e*, papillæ on the ridges; *f*, fat-clusters; *g*, sweat-glands; *h*, sweat-ducts; *i*, their openings on the surface.

The **True Skin, Cutis Vera, Derma,** or **Corium,** is a sentient and vascular fibrous texture. It is covered and defended, as already explained, by the non-vascular cuticle, and is attached to the parts beneath by a layer of areolar tissue, named "subcutaneous," which, excepting in a few parts, contains fat, and has therefore been called also the "panniculus adiposus" (fig. 471, *d*). The connection is in many

parts loose and moveable, in others close and firm, as on the palmar surface of the hand and the sole of the foot, where the skin is fixed to the subjacent fascia by numerous stout fibrous bands, the space between being filled with a firm padding of fat. In some regions of the body the skin is moved by striated muscular fibres, which may be unconnected with fixed parts, as in the case of the orbicular muscle of the mouth, or may be attached beneath to bones or fasciæ, like the other cutaneous muscles of the face and neck, and the short palmar muscle of the hand.

Structure.—The cutis vera is made up of an extremely strong and tough framework of interlaced connective tissue fibres. The fibres are chiefly of the white variety, such as constitute the main part of the fibrous and areolar tissues, and are arranged in stout interlacing bundles, except at and near the surface, where the texture of the corium becomes finer and closer. With these are mixed elastic fibres, which vary in amount in different parts, and connective tissue corpuscles, which are often flattened up against the bundles of white fibres. Towards the attached surface the texture becomes much more open, with larger meshes, in which lumps of fat and the sweat-glands are lodged ; and thus the fibrous part of the skin, becoming more and more lax and more mixed with fat, blends gradually with the subcutaneous areolar tissue.

In consequence of this gradual transition of the corium into the subjacent tissue, its thickness cannot be assigned with perfect precision. As a general rule, it is thicker on the posterior aspect of the head, neck, and trunk, than in front ; and thicker on the outer than on the inner side of the limbs, and as well as the cuticle, it is remarkably thick on the soles of the feet and palms of the hands. The skin of the female is thinner than that of the male.

The skin is generally said to measure from $\frac{1}{50}$th of an inch to nearly $\frac{1}{8}$th of an inch (·5 to 3 millimeters) ; but it has been pointed out by Warren that, on the back and shoulders, it may be as thick as 5 or 6 mm. ; and here it is almost entirely formed of dense anastomosing bundles of connective tissue, sending down on the one hand fibrous prolongations through the subjacent panniculus adiposus, and being penetrated obliquely on the other hand by columns of fat cells, which extend from that layer to the bases of the small hair-follicles, and conduct blood-vessels to these and to the surface of the skin.

Bundles of plain muscular tissue are distributed in the substance of the corium wherever hairs occur ; their connection with the latter will be afterwards explained. Muscular bundles of the same kind are found in the subcutaneous tissue of the scrotum, penis, perineum, and areola of the nipple, as well as in the nipple itself. They join to form reticular layers, attached to the under-surface of the corium. In the areola they are disposed circularly.

For convenience of description it is not unusual to speak of the corium as consisting of two layers, the "reticular" and the "papillary." The former, the more deeply seated, takes no part in the construction of the papillæ, but contains in its meshes hair-follicles, cutaneous glands, and fat. The latter is extended into papillæ, and receives only the upper portion of the hair-follicles and glands, together with the terminal expansion of the blood-vessels.

The free surface of the cutis vera is marked in various places with larger or smaller furrows, which also affect the superjacent cuticle. The larger of them are seen opposite the flexures of the joints, as those so well known in the palm of the hand and at the joints of the fingers. The finer furrows intersect each other at various angles, and may be seen almost all over the surface ; they are very conspicuous on the back of the hands. Fine curvilinear ridges, with intervening furrows, mark the skin of the palm and sole ; these are produced by the ranges of papillæ, to be immediately described : they form definite patterns, characteristic of each individual, but at the same time capable of being classified under a relatively small number of heads. Moreover, these patterns are permanent and do

not alter as growth advances, the impression obtained from the hand of a young child being identical even in the most minute details (although of course somewhat less displayed) with that obtained from the same individual when grown up (F. Galton).

Papillæ.—The free service of the corium is beset with small eminences thus named, which seem chiefly to contribute to the perfection of the skin as an organ of touch, seeing that they are highly developed where the sense of touch is exquisite. They serve also to extend the surface for the production of the cuticular tissue, and hence are large-sized and numerous under the nail. The papillæ are large, and in close array on the palm of the hand and palmar surface of the fingers, and on the corresponding parts of the foot. In these places they are ranged in lines forming the characteristic curvilinear ridges seen when the skin is still covered with its thick epidermis. They are of a conical figure, rounded or blunt at the top and sometimes cleft into two or more points when they are named compound papillæ. They are received into corresponding pits on the under-surface of the cuticle. In

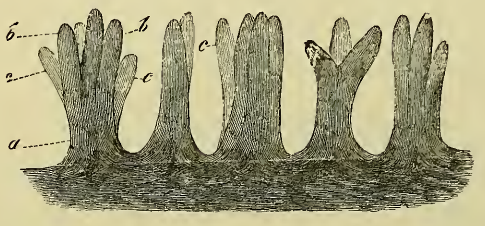


Fig. 472.—Magnified view of four of the ridges of the epidermis, with short furrows or notches across them: also the openings of the sudoriferous ducts. (After Breschet.)

Fig. 473.—Compound papillæ from the palm of the hand, magnified 60 diameters.

a, basis of a papilla; *b*, *b*, divisions or branches of the same; *c*, *c*, branches belonging to papillæ of which the bases are hidden from view. (After Kölliker.)

structure they resemble the rest of the superficial layer of the corium, and consist of a finely fibrillated tissue, with a few elastic fibres. The bundles of fibrils chiefly run parallel to the axis of the papilla and the fibrils appear to end near its surface, which has a somewhat corrugated aspect. On the palm, sole, and nipple, where they are mostly of the compound variety, they measure from $\frac{1}{200}$th to $\frac{1}{100}$th of an inch (0·125 to 0·25 mm.) in height. In the ridges, the larger papillæ are placed sometimes in single but more commonly in double rows, with smaller ones between them (fig. 471), that is, also on the ridges, for there are none in the intervening grooves. These ridges are marked at short and tolerably regular intervals with notches or short transverse furrows, in each of which, about its middle, is the minute funnel-shaped orifice of the duct of a sweat-gland (fig. 472). In other parts of the skin endowed with less tactile sensibility, the papillæ are broader, shorter, fewer in number, and irregularly scattered. On the face they are reduced to from $\frac{1}{800}$ to $\frac{1}{500}$ of an inch; and here they at parts disappear altogether, or are replaced by slightly elevated reticular ridges. Fine blood-vessels enter most of the papillæ, forming either simple capillary loops in each, or dividing into two or more capillary branches, according to the size of the papilla and its simple or composite form. Other papillæ receive nerves, to be presently noticed.

Blood-vessels and lymphatics.—The arteries divide in the subcutaneous tissue, and, as their branches pass from this deep expansion towards the surface of the skin, they supply offsets to the fat-clusters, sweat-glands, and hair-follicles. They divide and anastomose again near the surface, and at length, on reaching it, form a network of capillaries, with polygonal meshes. Fine looped branches pass

from the superficial arteries into the papillæ, as already mentioned. The veins closely accompany the arteries.

Lymphatics are found in all parts, although probably not everywhere in equal number; they are abundant and large in some parts of the skin, as on the scrotum and round the nipple. They form at least two networks, one superficial and another more deeply situated, which intercommunicate by uniting vessels, whilst the deeper network joins the lymphatics of the subcutaneous tissue. According to Klein there is a continuous plexus through the whole thickness of the corium, and all the vessels possess valves. The most superficial network, although close to the surface of the corium, is beneath the net of superficial blood-capillaries, which are much smaller than the lymphatic capillaries. In certain parts on the palm and sole lymphatics pass into the papillæ, but do not reach their summits. Other lymphatics accompany the blood-vessels, two passing commonly with each small artery and vein, and joining and anastomosing over the vessels.

As in other kinds of connective tissue, the lymphatics of the skin may be said to originate in the cell-spaces of the tissue, and since the cells lie for the most part in rows between the bundles, the combined spaces form interfascicular clefts which can be injected with the lymphatics. The superficial cell-spaces communicate with the intercellular channels of the epithelium, and thus these also are brought into connection with the lymphatics. The cell-spaces of the adipose tissue can similarly be injected.

Nerves.—Fine varicose nerve-fibrils pass up into the epidermis, penetrating between the cells of the Malpighian layer (fig. 474), where they undergo a certain amount of ramification. The branches do not unite with one another to form a network, but end in knob-like swellings or varicosities. With the growth and displacement of the cells between which they are placed, these varicosities become, according to Ranvier, continually detached from the end of the fibrils, the latter meanwhile growing constantly to supply the place of the detached portions.

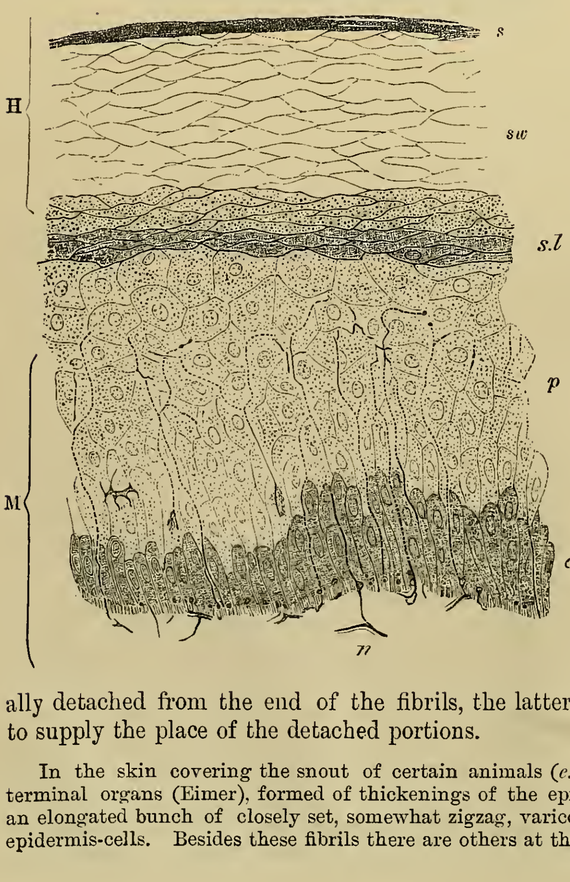


Fig. 474.—Section of epidermis from the human hand. Highly magnified. (Ranvier.)

H, horny layer, consisting of *s*, superficial horny scales; *sw*, swollen-out horny cells; *s.l*, stratum lucidum; *M*, rete mucosum or Malpighian layer, consisting of *p*, prickle-cells, several rows deep; and *c*, elongated cells forming a single stratum near the corium; *n*, part of a plexus of nerve-fibres in the superficial layer of the cutis vera. From this plexus, fine varicose nerve-fibrils may be traced passing up between the cells of the Malpighian layer.

In the skin covering the snout of certain animals (*e.g.* mole) the nerves end in peculiar terminal organs (Eimer), formed of thickenings of the epidermis, the nerve-fibres passing as an elongated bunch of closely set, somewhat zigzag, varicose, unbranched fibrils between the epidermis-cells. Besides these fibrils there are others at the periphery of the organ which are

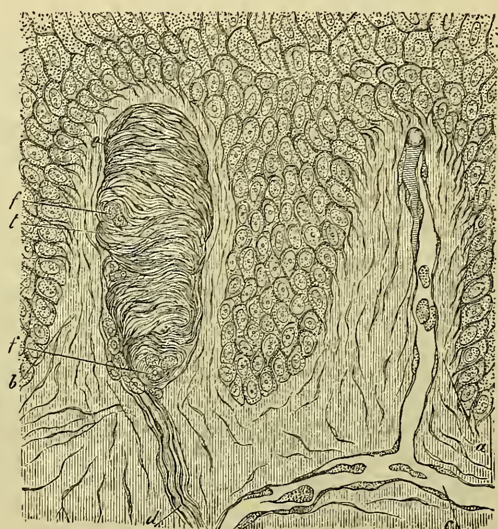
less closely arranged, and terminate in branched extremities as in other parts of the epidermis. In the snout of the pig the branched axis cylinders pass partly into concavo-convex enlargements between the deeper epithelium cells (tactile menisci of Ranvier, see p. 335).

Merkel has described the nerves of the epidermis as ending in pyriform cells (tactile cells) placed between the ordinary epithelial cells ; and Langerhans thought that the nerves could be traced to stellate cells in the interstitial spaces, but improved methods of staining with chloride of gold, which have been employed in the investigation, would seem to render it probable that the termination of the nerve-fibrils in the cuticle is free as above described, and *between* the cells, not actually within them.

Nerves are supplied in very different proportions to different regions of the true skin. They pass upwards towards the papillary surface, where they form plexuses, of which the meshes become closer as they approach the surface, and the constituent branches finer. From the most superficial or subepithelial plexus, which lies immediately under the epithelium, delicate non-medullated fibrils pass upwards amongst the cells of the Malpighian layer of the epidermis, where they end, as we have seen, in free extremities. A large share of the nerves of the cutis vera is distributed to the hair-follicles, whilst some terminate in end-bulbs, tactile corpuscles, and Pacinian bodies, the last-named being seated in the subcutaneous tissue. The tactile corpuscles of the skin are found most numerously in certain papillæ of the palm and sole, more sparingly in those of the back of the hand and foot, the palmar surface of the fore-arm, and the nipple. Such papillæ commonly contain no blood-vessels, and are named "tactile" (fig. 475, *b*), as distinguished from the "vascular" papillæ (*a*). The structure of these different terminal corpuscles has been already described (pp. 332 to 344). Many of the nerve-fibres, probably chiefly the non-medullated, are supplied to the plain muscular tissue of the minute hair-muscles, and to that of the blood-vessels.

Fig. 475.—Section of skin showing two papillæ and deeper layers of epidermis. (Biesiadecki.)

a, Vascular papilla with capillary loop passing from subjacent vessel *c* ; *b*, nerve papilla with tactile corpuscle, *t*. The latter exhibits transverse fibrous markings : three nerve-fibres, *d*, are represented as passing up to it : at *f f* these are seen in optical section.



NAILS AND HAIRS.

The nails and hairs are growths of the epidermis, agreeing essentially in nature with that membrane.

Nails.—The posterior part of the nail, which is concealed in a groove of the skin, is named its "root," the uncovered part is the "body," which terminates in front by the "free edge." A small portion of the nail near the root, named from its shape the *lunula*, is whiter than the rest. This appearance is due to the substance of the nail at this point possessing a greater degree of opacity in consequence of its being covered with a thick layer of the rete mucosum, the cells of which are in active process of division (Toldt).

The part of the corium to which the nail is attached, and by which in fact it is secreted or generated, is named the *matrix.* This portion of the skin is highly vascular and thickly covered with large vascular papillæ. Posteriorly the matrix forms a crescentic groove or fold, deep in the middle but getting shallower at the

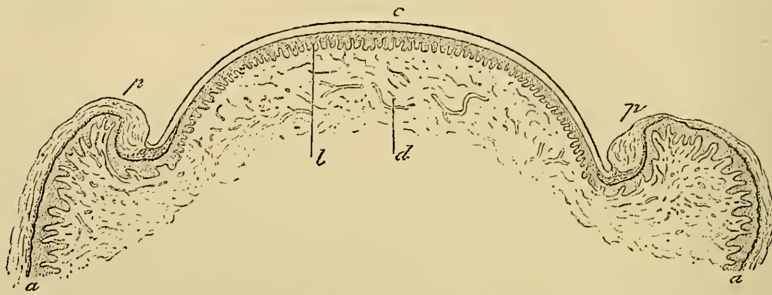


Fig. 476.—Section across the middle of the nail of a child of 8 days. (Ranvier.)

c, body of the nail ; *l*, nail-bed with its papillated ridges and rete mucosum ; *d*, corium under nail-bed ; *p*, fold at edge of nail : here the horny layer is separated from the mucous layer by a well marked stratum granulosum, which is altogether lacking over the nail-bed ; *a*, skin of finger at side of nail.

sides, which lodges the root of the nail ; the rest of the matrix, before the groove, is usually named the *bed* of the nail. The small lighter-coloured part of the matrix nearest the groove and corresponding with the lunula of the nail, is covered with papillæ having no regular arrangement, but the whole remaining surface of the

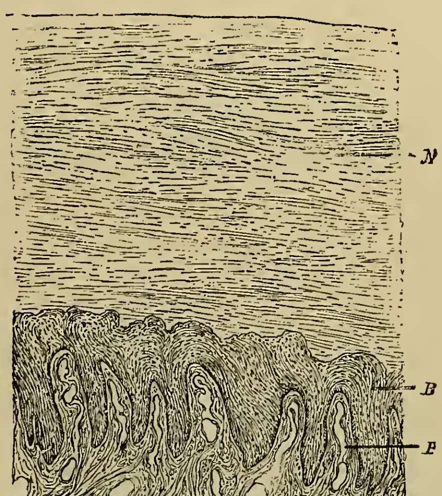


Fig. 477.—Section across the nail and nail-bed. (Heitzmann).

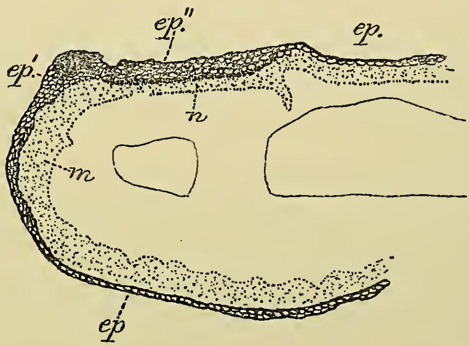
P, papillæ ; *B*, rete mucosum of nail-bed ; *N*, nail.

matrix situated in front of this, and supporting the body of the nail, is marked with longitudinal ridges. These ridges are cleft at their summits into rows of papillæ, which are directed obliquely forwards and are better marked towards the distal end of the nail. The ridges, or *laminæ*, as they are sometimes, and perhaps more suitably, named, fit into corresponding furrows on the under-surface of the nail-epidermis. At the posterior part of the matrix they are low, but increase in height anteriorly.

The nail, like the cuticle, is made up of epithelial cells. The oldest and most superficial of these are the broadest and hardest, but at the same time very thin, and so intimately connected together that their respective limits are scarcely discernible. They form the exterior, horny part or nail proper, and cohere together in irregular layers. On the other hand, the youngest cells, which are those situated at the root and under-surface, are softer and of a polygonal shape. The deepest layer differs somewhat from the others, in having its cells elongated, and

arranged perpendicularly, as in the case of the epidermis. Thus the under part of the nail (fig. 477, B) corresponds in nature with the Malpighian or mucous layer of the epidermis, and the upper part (C) with the horny layer. The most superficial cells of the Malpighian layer of the nail have a granular aspect, but this is due according to Kölliker not to the presence of actual granules, but to the spiny processes which unite them to one another. As in the case of epidermis, the hardened scales of the nails may be made to reassume their cellular character by treatment with caustic alkali, and afterwards with water: and then it is seen that they still retain their nuclei.

Formation and growth of the Nails.—In the third month of intra-uterine life, the part of the embryonic corium which becomes the matrix of the nail is marked off by the commencing curvilinear groove, which limits it posteriorly and laterally.



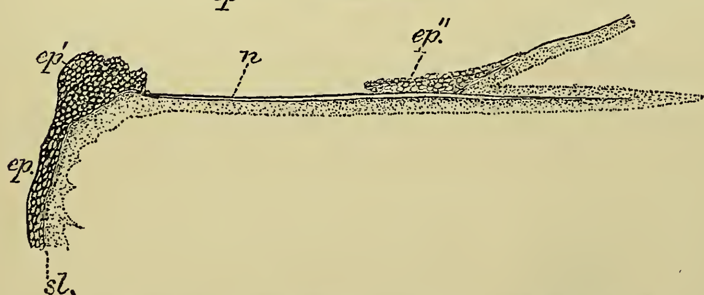


Fig. 478.—Longitudinal section of the terminal phalanx of the third finger of an embryo of the third month. Somewhat magnified. (After Bowen.)

ep, epitrichial cells, greatly multiplied at the nail-edge *ep'*, and forming the eponychium *ep''* above the nail formation, *n*.

Fig. 479.—Longitudinal section of the great toe of an embryo of the fifth month. Somewhat magnified. (After Bowen.)

ep, epitrichial layer; *ep'*, thickening of epitrichium at the nail edge; *ep''*, remains of eponychium; *n*, nail; *s.l.*, stratum lucidum.

The epidermis on the matrix then begins to assume, in the under part of its horny layer, the characters of a nail, which may, therefore, be said to be at first embedded in the embryonic cuticle, forming a highly developed stratum lucidum. The nail rudiment, which is preceded by and apparently formed from a layer of eleidin-cells (fig. 478, *n*), first appears near the posterior part of the matrix, and grows forward from this over the bed and backwards into the groove. After the end of the fifth month it becomes free at the anterior border, breaking through the thick layer of epidermis (eponychium) which covers it superficially. The remains of this layer continue throughout life partly covering the lunula. At the anterior edge of the

developing nail the superficial layer of the epidermis or epitrichial layer (*vide ante*, p. 412) is greatly thickened, and below this thickening is a well-marked stratum lucidum and subjacent granular layer. Before the anterior border of the nail becomes free, it appears to be continuous with the stratum lucidum in front of it. At birth the free end is long and thin, being manifestly the earlier formed part which has been pushed forward. As the infantile nail continues to grow, its flattened cells, at first easily separable, become harder and more coherent, as in after-life.

The average rate of growth of the nails is about $\frac{1}{32}$ of an inch per week.

The growth of the nail is effected by a constant generation of the cells of the Malpighian layer at the root. These cells acquire eleidin granules, and each successive series being followed and pushed from their original place by others, they become flattened into dry, hard, and inseparably coherent scales. By this addition of new cells at the posterior edge the nail is made to advance, and by the apposition of similar particles to its under-surface at the lunula, it grows in thickness; so that it is thicker at the anterior border of the lunula than nearer the root. It does not appear to increase in thickness while passing over the bed. When a nail is thrown off by suppuration, or pulled away by violence, a new one is produced in its place, provided any of the cells of the deeper layers of the epithelium are left.

Hairs.—A hair consists of the root, which is fixed in the skin, and the shaft or stem. The stem is generally cylindrical, but may be more or less flattened: when the hair is young, it becomes gradually smaller towards the point. The length and thickness vary greatly in different individuals and races of mankind as well as in different regions of the body. In the straight-haired races (*e.g.* Mongolian), the individual hairs are coarser and thicker and the section more circular than in the crisp-haired races (negro) in which the section is smaller and oval, the hairs being sometimes markedly flattened. The section is largest in the North American Indians, Chinese, and especially in the Japanese. Light-coloured hair is usually finer than black.

The stem is covered with a coating of finely imbricated scales, the upwardly projecting edges of which give rise to a series of fine waved transverse lines, which

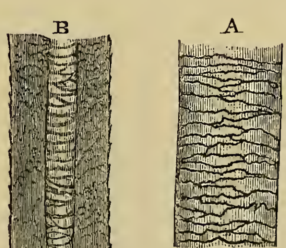


Fig. 480.—Human hair. (E. A. S.)

A, The surface of the hair focussed to show the cuticular scales. *B*, optical section. The medulla looks clear, the air having been expelled from it by Canada balsam.

may be seen with the microscope on the surface of the hair (fig. 480, A). Within this scaly covering, called the *hair-cuticle*, is a *fibrous* or *cortical substance* which in all cases constitutes the chief part and often the whole of the stem; but in many hairs the axis is occupied by a substance of a different nature, called the *medulla* or *pith*. The *fibrous substance* is translucent, with short longitudinal opaque streaks of darker colour intermixed. It is formed of straight, rigid, longitudinal fibres, which again may be resolved into flattened cells of a fusiform outline; they may be marked with ridges and furrows, and united with one another by fibrils, as with the deeper cells of stratified epithelium (Waldeyer). The colour of the fibrous substance is caused by oblong patches of pigment-granules, and generally diffused colouring matter of less intensity. Very slender elongated nuclei are also discovered by means of reagents, whilst specks or marks of another description in the fibrous substance are occasioned by minute irregularly-shaped cavities containing air. These air-lacunules are abundant in white hairs, and are best seen in them, there being no risk of deception from pigment-specks; indeed they may be altogether

wanting in very dark hairs. Viewed by transmitted light they are dark, but brilliantly white by reflected light. When a white hair has been boiled in water, ether, or oil of turpentine, these cavities become filled with fluid, and are then quite pellucid ; but when a hair which has been thus treated is dried, the hair quickly finds its way again into the lacunæ, and they resume their original aspect.

The *medulla* or *pith*, as already remarked, does not exist in all hairs. It is wanting in the fine hairs over the general surface of the body, and is not commonly met with in those of the head, nor in the hairs of children under five years. When present

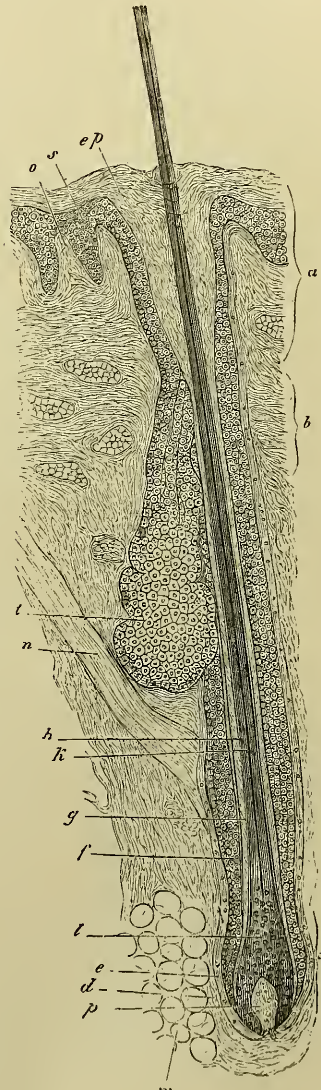


Fig. 481.—Hair-follicle, in longitudinal section. Moderately magnified. (Biesiadecki.)

a, mouth of the hair-follicle ; *b*, its neck ; *c*, lower bulbous enlargement ; *d*, *e*, dermic coat (outer and inner layers, the innermost or hyaline layer is not shown) ; *f*, *g*, epidermic coat (outer and inner root-sheath) ; *h*, fibrous substance of the hair ; *k*, medulla ; *l*, hair-knob ; *m*, fat in the subcutaneous tissue ; *n*, arrector pili ; *o*, papilla of the cutis ; *p*, papilla of the hair-knob ; *s*, Malpighian layer of the epidermis ; *ep*, horny layer, incorrectly represented in the figure as continuous with the inner root-sheath ; *t*, sebaceous gland.

it occupies the centre of the shaft and ceases towards the point. It is composed of rows of cells, differing in shape, but generally angular, and in many animals exhibiting regular patterns. When viewed by transmitted light, it is black ; by reflected light, on the other hand, it is white, its colour being chiefly due to the contained air-particles which lie in spaces between the cells, but in the hairs of a few animals are within the cells. They are produced by the drying of the originally soft cells of the medulla, on the exposure of the growing hair to the atmosphere. The medulla may be interrupted at parts for a greater or less extent. In the latter case, the axis of the stem at the interruptions is fibrous like the surrounding parts.

The **root** of the hair is lighter in colour and softer than the stem ; in young and growing hairs it swells out at its lower end into a bulbous enlargement or knob (figs. 481, 483), but in older hairs which have ceased to grow and are in process of being shed, the termination of the root is not bulbous (fig. 488). The root of the hair is received into a recess of the skin named the *hair-follicle*, which, when the hair is of considerable size, reaches down into the subcutaneous fat.

The substance of the hair, of epidermic nature, is, like the epidermis itself, quite extra-vascular, but like that structure also, it is organised and subject to internal organic changes. Thus, in the progress of its growth, the cells change their figure, and acquire greater consistency. In consequence of their elongation, the hair, bulbous at the commencement, becomes reduced in diameter, and cylindrical above. But it cannot be said to what precise distance from the root organic changes may extend. Some have imagined that the hairs are slowly permeated by a fluid from the root to the point, but this has not been proved. The sudden change of the colour of the hair from dark to grey, which sometimes happens, has never been

satisfactorily explained : it appears generally to be due to the development of air between the elongated cells composing the hair.

The rate of growth of hair is about half-an-inch a month.

Hairs are found on all parts of the skin except the palms of the hands and soles of the feet, the dorsal surface of the third phalanges of the fingers and toes, the glans, and the inner surface of the prepuce. On the scalp they are set in groups, on the rest of the skin for the most part singly. Except those of the eyelashes, which are implanted perpendicularly to the surface, they have usually a slanting direction, which is constant in the same parts. In the negro the hair-follicles have been found to be curved, so that the papilla may look in a direction parallel to or even away from the surface of the skin (Stewart).

With the exception of the bones and teeth, no tissue of the body withstands decay after death so long as the hair, and hence it is often found preserved in sepulchres, when nothing else remains but the skeleton.

Structure of the hair-follicle.—The follicle, which receives near its mouth the opening ducts of one or more sebaceous glands (fig. 481, *t*), consists of an outer coat continuous with the corium, and an epidermic lining continuous with the cuticle.

The outer or *dermic* coat of the follicle is thin but firm, and consists of three layers. The most external (fig. 482, *a*) is formed of connective tissue in longitudinal bundles, without elastic fibres, but with numerous corpuscles. It is highly vascular, and provided with nerves. It is continuous above with the corium, and determines the form of the follicle. The most internal layer (*hyaline layer*, Kölliker) (fig. 482, *d*) is a transparent homogeneous membrane, marked transversely on its inner surface with some raised lines, and not reaching so high as the mouth of the follicle ; it corresponds with the membrana propria or basement membrane of allied structures. Between the two is a layer extending from the bottom of the follicle as high as the entrance of the sebaceous glands, composed of an indistinctly fibrous matrix, which tears transversely, and of transversely disposed connective tissue corpuscles, with oblong nuclei (fig. 482, *c*). This layer is continuous with the papillary part of the cutis vera, and its blood-vessels are continuous above with those of that layer.

The *epidermic coat* of the follicle adheres closely to the root of the hair, and commonly separates, in great part, from the follicle and abides by the hair when the

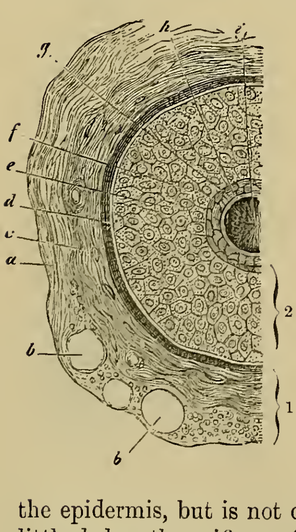


Fig. 482.—Section of hair-follicle. (Biesiadecki.)

1, Dermic coat of follicle ; 2, epidermic coat or root-sheath : *a*, outer layer of dermic coat, with blood-vessels, *b*, *b*, cut across ; *c*, middle layer ; *d*, inner or hyaline layer ; *e*, outer root-sheath ; *f*, *g*, inner root-sheath ; *h*, cuticle of root-sheath ; *i*, hair.

latter is pulled out; hence it is sometimes named the "root-sheath." It consists of an outer, softer, and more opaque stratum (fig. 428, *e*), next to the dermic coat of the follicle, and an internal more transparent layer (fig. 482, *f*, *g*) next to the hair. The former, named also the *outer root-sheath*, and by much the thicker of the two, corresponds with the Malpighian layer of the epidermis in general, and contains soft polygonal cells, including pigment-granules in the coloured races, which at the lower part form a much thinner stratum and pass continuously into those of the hair-knob ; the internal layer or *inner root-sheath*, probably represents the stratum lucidum of the epidermis, but is not continuous with that part of the skin, ceasing abruptly a little below the orifices of the sebaceous ducts. Lining the root-sheath internally is a layer of imbricated, downwardly-projecting scales, the *cuticle of the root-sheath* (fig. 482, *h*), which is applied to the cuticle of the hair proper, to whose upwardly directed scales it fits like a mould. Its scales, as well as those of the hair-cuticle,

pass, at the bottom of the follicle, into a layer of columnar cells which covers the surface of the hair-knob. The inner root-sheath itself consists of two layers, which towards the bottom of the follicle become blended into one. The innermost (that

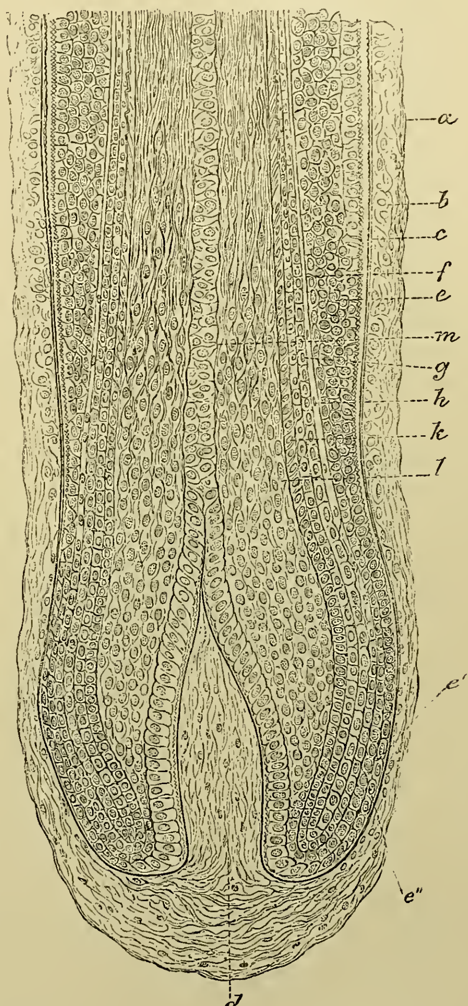


Fig. 483.—Longitudinal section through the fundus of a hair-follicle of the human scalp. (Mertsching.)

a, outer, longitudinal layer of the dermic coat; *b*, inner, circular layer; *c*, hyaline layer, which seems to be formed of two layers; *d*, papilla, somewhat prolonged amongst the cells from which the medulla is forming: this is not an uncommon condition; *e*, outer root-sheath, composed near the bottom of the follicle of only two layers of cells, of which the outer *e′* is the direct prolongation of the columnar cells, while the inner *e″* is in contact with Henle's layer and is formed of more flattened cells: both pass over the papilla into the cells of the hair-bulb; *f*, Henle's sheath, showing nuclei only below at the level of the papilla: at the bottom of the follicle it is continuous with the cells of the hair-cuticle, *k*; *g*, Huxley's layer, passing round into continuity with the cuticle of the root-sheath, *h*; *l*, cells which are becoming transformed into the hair-cortex; *m*, medulla becoming formed from the cells which immediately cap the papilla.

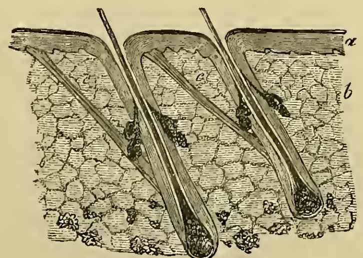
next the cuticula) is known as *Huxley's layer;* it consists of flattened polygonal nucleated cells, two or three deep. The outermost (*Henle's layer*) is composed of oblong, somewhat flattened cells without nuclei, between which gaps frequently occur, so as to give it the aspect of a perforated membrane. These gaps are filled up by projections from the cells of Huxley's layer. At the lower part both layers pass into a single stratum of large polygonal nucleated cells without openings between them. At the upper part also of the follicle the two layers of the inner root-sheath are not distinguishable from one another (Ebner).

The soft, bulbous enlargement of the root of the growing hair is formed of cells which are in course of multiplication, and are not arranged in definite strata. Laterally they are continuous with the cells of the outer root-sheath. Superficially they are becoming gradually transformed into the horny cells of the hair and of the inner root-sheath. At the bottom of the follicle they rest upon the hair-papilla, which may send a delicate extension between them. The papilla, which is vascular and also receives nerves, rises up into the bottom of the follicle, fitting into a corresponding excavation of the hair-knob. In the large tactile hairs of animals it is very conspicuous. As the follicle, in short, is a recess of the corium, so the hair-papilla is a cutaneous papilla rising up in the bottom of it.

Nerves of the hairs.—Nervous branches pass to the hair-follicles, and some, as just remarked, enter the papilla; but besides these, many fibres pass into the outer root-sheath, where they appear to end as in the Malpighian layer of the

epidermis. In the tactile hairs of animals, the nerves were described by Schöbl as passing upwards over the outer root-sheath, losing their white substance, and forming a close plexus with vertical meshes ; finally ending in an annular expansion, which encircles the hair just below the orifices of the sebaceous glands, and is in immediate connection with the hyaline layer of the follicle. This statement has been generally confirmed, except that the annular expansion of Schöbl has been shown to be an annular ramification of pale fibres amongst the cells of the outer root-sheath, some of the nerve-fibres becoming more superficial again and terminating in irregular, disk-like enlargements between the root-sheath and the hyaline layer. Ordinary hairs receive fewer nerve-fibres, but, as in the tactile hairs, most of these appear to end in the outer root-sheath at about the level of the orifices of the sebaceous glands. In the larger tactile hairs the bulb is surrounded by cavernous tissue, which lies between the outer and middle layers of the dermic coat.

Muscles of the hairs.—Slender bundles of plain muscular tissue (arrectores pili) are connected with the hair-follicles (figs. 481, 484). They arise, generally, by a number of fasciculi, from the most superficial part of the corium, and joining to form a somewhat flattened and plexiform muscle they pass down obliquely to be inserted into the outside of the follicle below the sebaceous glands, which they in a



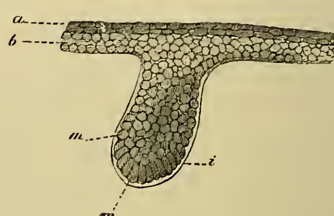


Fig. 484.—Section of the skin of the head, with two hair-follicles. Diagrammatic. (Kölliker.)

a, epidermis ; *b*, corium ; *c*, muscles of the hair-follicles.

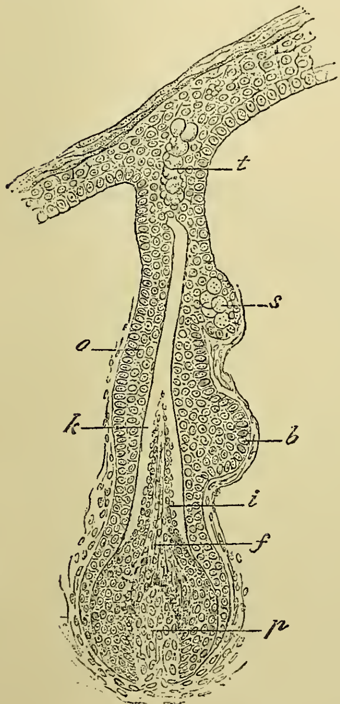
Fig. 485.—Hair-rudiment from an embryo of six weeks, magnified 350 diameters. (Kölliker.)

a, horny, and *b*, mucous or Malpighian layer of cuticle ; *i*, limitary membrane ; *m*, cells (some of which are assuming an oblong figure) which chiefly form the future hair.

measure embrace in their passage. In the dermic coat of the follicle some of the muscular fibres become transverse, and partly encircle the lower part of the follicle. They are placed on the side to which the hair slopes, so that their action in elevating the hair is evident. When the hairs are in groups, as in the scalp, one muscle may divide as it passes to its insertion, and may be attached to several follicles (Hesse). In some parts a muscular slip is sent more deeply into the integument and becomes attached to the connective tissue which encloses a sweat-gland.

Development of hair in the fœtus.—The rudiments of the hairs may be discerned at the end of the third or beginning of the fourth month of intra-uterine life, as little black specks beneath the cuticle. They are formed of down-growths of the Malpighian layer, which sink into the corium (fig. 485). A homogeneous limiting membrane is seen (*i*), inclosing the collection of cells, and continuous above with a similar simple film which at this time lies between the cuticle and the corium ; it becomes the innermost or hyaline layer of the dermic coat of the follicle. The hair-rudiment next lengthens and swells out at the bottom, so as to assume a flask-shape, and it is now found fitted over a papilla which has become formed in the subjacent corium. Outside the limitary membrane, the fibres, corpuscles, and other constituents of the dermic coat of the follicle become formed. While this is

going on outside, the cells within the follicle which at first were uniform in appearance, are found to have undergone changes, having become transformed into the layers of the root-sheath and the miniature conical hair. The inner root-sheath, lying next to the hair (fig. 486, *k*), is distinguished by its translucency from the more opaque outer part that fills up the rest of the cavity. The hair and the inner root-sheath are formed from the cells which cover the top of the papilla. These appear to acquire eleidin-granules, and also, in the case of those which produce the hair, pig-



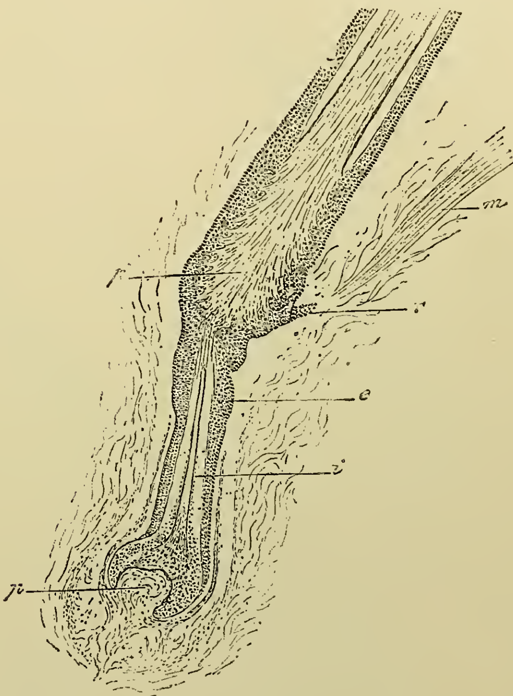


Fig. 486.—Developing hair from a human embryo of $4\frac{1}{2}$ months. (Ranvier.)

p, papilla ; *f*, hair-rudiment ; *i*, cells forming inner root-sheath ; *k*, keratinized portion of inner root-sheath, remaining uncoloured by carmine ; *e*, external root-sheath ; *b*, epithelial bed, for insertion of arrector pili ; *s*, sebaceous gland ; *t*, sebaceous matter forming independently in the part which will become the neck of the follicle.

Fig. 487.—Replacement of old hair by a newly developing one in the human scalp. (Ranvier.)

p, papilla of the new hair ; *i*, its inner root-sheath ; *e*, its outer root-sheath continuous above with that of the old hair, *p′* ; *r*, epithelial projection at the level of the insertion of the arrector pili, *m*.

ment-granules ; the eleidin-granules are stated to be most abundant in the cells which form the medulla of the hair and in those which form the inner root-sheath.

As the young hair reaches in its growth the upper part of the follicle, the central cells which block the neck of the follicle undergo a kind of fatty degeneration, and disintegrate to produce a sebaceous secretion like that of the sebaceous glands (fig. 486, *t*). The latter in the meantime are becoming formed as extensions of the outer root-sheath of the hair laterally into the corium (*s*), and they soon open into the neck of the follicle.

Between the soft cells of the hair-bulb in the growing hair there are frequently seen wander-cells, which contain pigment-granules, and it is supposed that the pig-

ment may be carried to the cells of the hair-bulb through their agency (Riehl). The young hair continuing to grow, at last perforates the cuticle, either directly, or after first slanting up for some way between the mucous and horny strata : it is often bent like a whip, and then the doubled part protrudes.

The first hairs produced constitute the *lanugo;* their eruption takes place about the fifth month of intra-uterine life, but some of them are shed before birth, and are found floating in the liquor amnii.

According to Kölliker's observations, the infantile hairs are entirely shed and renewed within a few months after birth ; those of the general surface first, and afterwards the hairs of the eyelashes and head, which he finds in process of change in infants about a year old. A formation of new hairs, preceded or accompanied by a shedding of the old ones, also goes on during the whole of life. The papilla of the

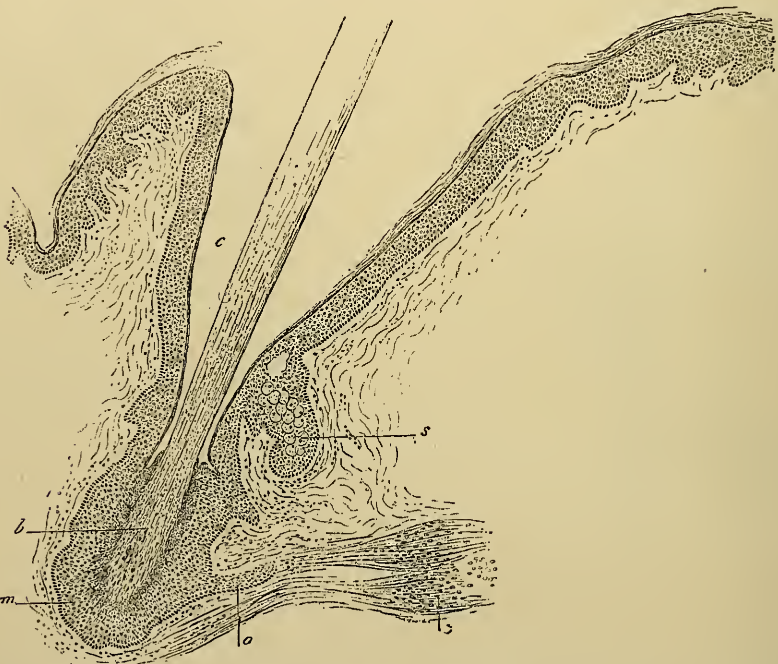


Fig. 488.—Longitudinal section through the follicle of a hair which has ceased growing. (Ranvier.)

m, epithelium at the bottom of the follicle (which contains no papilla) ; *b*, modified hair-bulb ; *c*, neck of the hair-follicle somewhat opened in preparing the section ; *s*, sebaceous gland ; *o*, epithelial bud at the level of the insertion of the arrector pili.

old hair atrophies and the hair-bulb disappears (fig. 488). The hair-root acquires a closer attachment to the sides of the follicle within which it gradually becomes shifted towards the surface of the skin, but all active growth ceases, and finally the hair drops out of the follicle. The new hairs are generated in the follicles of the old (fig. 487). An increased growth of cells takes place at one part, usually the bottom of the follicle, and a new papilla is produced within the mass of cells thus formed. These cells occupying the lower part of the follicle, and resting on the papilla, are gradually converted into a new hair with its root-sheath, just as in the primitive process of formation in the embryo.

The **sebaceous glands** (figs. 481, 489) are small saccular glands which pour out their secretion at the roots of the hairs, for, with very few exceptions (labia

minora, and, in some individuals, at the red margin of the lips, near the angle of the mouth), they open into the hair-follicles, and are found wherever there are hairs. Each has a short duct, which opens at a little distance within the mouth of the hair-follicle, and by its other end, leads to a cluster of small rounded secreting saccules, which as well as the duct are lined by epithelium (fig. 489), usually charged with the fatty secretion. The cells as they multiply and become filled with the fatty granules advance to the lumen of the alveoli. Here they become disintegrated, and the fatty and other matters with which they are charged form the secretion of the gland, which is discharged by the duct into the mouth of the hair-follicle. The number of saccular recesses connected with the duct usually varies from four or five to twenty; it may be reduced to two or three, in very small glands, or even to one, but this is rare. These glands are lodged in the substance of the corium. They are usually placed on the side to which the hair slopes, and in the angle formed by the junction of the arrector pili with the hair, so that when the muscular fibres contract they tend to compress the gland. Several may open into the same hair-follicle, and their size is not regulated by the magnitude of the hair. Thus, some of the largest are connected with the fine downy hairs on the alæ of the nose and other parts of the face, and there they often become unduly charged with pent-up secretion.

Fig. 489.—Longitudinal section of a sebaceous gland from the cheek with a small hair growing through its duct. Human. (Toldt.)

The Meibomian glands of the eyelids are regarded as modified sebaceous glands.

Development of the sebaceous glands.—The rudiments of the sebaceous glands sprout like little buds from the sides of the hair-follicles; they are at first, in fact, excrescences of the external root-sheath (fig. 486, *s*), and are composed entirely of similar cells. Each little process soon assumes a flask-shape and the central cells become occupied by fat particles. This fatty transformation of the cells extends itself along the axis of the pedicle until it penetrates through the root-sheath, and the fat-cells thus escape into the cavity of the hair-follicle, and constitute the first secretion of the sebaceous gland. They are soon succeeded by others of the same kind, and the little gland is established in its office. Additional saccules and recesses, by which the originally simple cavity of the gland is complicated, are formed by budding out of its epithelium, as the first was produced from the epithelial root-sheath, and are excavated in a similar manner.

The sudoriferous glands or sweat-glands (figs. 471 and 490).—These are seated on the under-surface of the corium, and at variable depths in the subcutaneous adipose tissue. To the naked eye they have the appearance of small round reddish bodies, each of which, when examined with the microscope, is found to consist of a tube, coiled up into a ball (though sometimes forming an irregular or flattened figure); from which the tube is continued, as the duct of the gland, upwards through the true skin and cuticle, and opens on the surface by a slightly widened orifice. The secreting tube is considerably larger than the duct, and also

has a much wider lumen (fig. 490). The duct, as it passes through the epidermis, is twisted like a corkscrew, that is, in parts where the epidermis is sufficiently thick to give room for this (fig. 466) ; lower down it is straight or but slightly curved. Sometimes the duct is formed of two coiled-up branches which join at a short distance from the gland. The tube, both in the gland and where it forms the excretory duct, has a vascular investment of connective tissue, continuous with the corium, and reaching no higher than the surface of the true skin, and within this investment consists of a thin membrana propria and an epithelial lining. The epithelium in the gland proper is formed of a single layer of cubical or columnar cells (often containing brownish pigment) and, in the duct, of two or more layers bounded next the

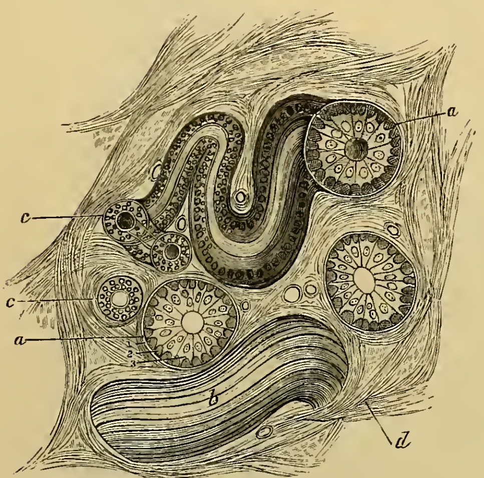


Fig. 490.—Section of a sweat-gland in the human skin. (E. A. S.)

a, *a*, secreting tube in transverse section ; *b*, part of secreting tube seen from above (surface focus) ; *c*, *c*, efferent tube (commencing duct) ; *d*, intertubular connective tissue with blood-vessels. In the section across the secreting tube 1 is the basement membrane ; 2, the muscular fibres cut across ; 3, the secreting epithelium lining the tube.

lumen by a fine cuticular lining. The epithelium of the duct is continuous with the epidermis, the twisted part of the duct being merely a channel excavated between the epidermis cells. In the proper secreting portion of the gland between the epithelium and the basement membrane, is a layer of longitudinally and obliquely disposed fibres which are generally described as plain muscular fibres, although the evidence of their muscular nature is not conclusive (Tartuferi). They vary in amount and are best marked in the larger glands, where they form a complete layer ; in smaller glands the layer is incomplete, and in the smallest the fibres may be altogether lacking. According to Bonnet the muscular layer is least developed in those parts of the skin which are most subject to the tension produced by contraction of ordinary muscles, and in those glands which yield a more fluid secretion. The fibres are absent in the duct. The latter is often coiled two or three times before leaving the gland, but its coils are distinguished from those of the gland proper by the differences above mentioned. The secreting cells of the sweat-glands show the peculiar striated structure characteristic of many gland-cells, and minute canals or clefts are said to pass from the lumen of the tube between the opposed surfaces of the cells (Ranvier). In the large glands in the axilla, at the root of the penis, on the labia majora, and in the neighbourhood of the anus, the layer of so-called muscular fibre-cells between the epithelium and basement membrane is very well marked. In the larger glands, also, the duct is rarely simple, being more usually parted by repeated dichotomous division into several branches, which before ending give off short cæcal processes ; in rare cases the branches anastomose. On carefully detaching the cuticle from the true skin, after its connection has been loosened by putrefaction, it usually happens that the cuticular linings of the sweat-ducts get separated from their interior to a certain depth, and are drawn out in form of short threads attached to the under surface of the epidermis. The coils of the gland-tube are loosely held together by connective tissue (fig. 490, *d*), which may form a sort of

capsule round the body of the gland. Each little sweat-gland is supplied with a dense cluster of capillary blood-vessels.

Distribution.—Sweat-glands exist most numerously in regions unprovided with hairs, but they occur in all parts of the skin, and may in some cases open into hair-follicles. According to Krause, nearly 2,800 open on a square inch of the palm of the hand, and somewhat fewer on an equal extent of the sole of the foot. He assigns rather more than half this number to a square inch on the back of the hand, and not quite so many to an equal portion of surface on the forehead, and the front and sides of the neck. On the breast, abdomen, and fore-arm, he reckons about 1100 to the inch, while on the lower limbs and the back part of the neck and trunk, the number in the same space is not more than from 400 to 600.

The **size** of the sweat-glands also varies. According to the observer last named, the average diameter of the coil is about $\frac{1}{70}$ inch; but in some parts they are larger than this—as, for example, in the groin, but especially in the axilla. In this last situation Krause found the greater number to measure from $\frac{1}{36}$ to $\frac{1}{12}$ inch, and some nearly $\frac{1}{6}$ inch in diameter.

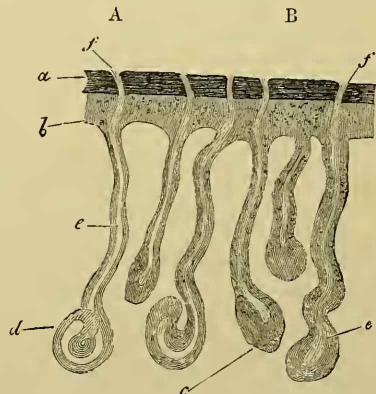


Fig. 491.—Developing sweat-glands from a seven months fœtus. Magnified 50 diameters. (Kölliker.)

a, horny layer of the epidermis; *b*, Malpighian layer; *d*, rudimentary gland; *e*, lumen of the duct, opening at *f* upon the surface of the skin.

The **development** of the sweat-glands has been carefully studied by Kölliker. Their rudiments, when first discoverable in the embryo, have much the same appearance as those of the hairs, and, in like manner, consist of processes of the mucous layer of the epidermis, which pass down and are received into corresponding recesses of the corium (fig. 491). They are formed throughout of cells collected into a solid mass of a club shape, continuous by its small end with the Malpighian layer of the epidermis, and elsewhere surrounded by homogeneous limiting membrane which is prolonged above between the corium and cuticle. The subsequent changes consist in the elongation of the rudimentary gland, the formation of a cavity along its axis—at first without an outlet—the prolongation of its canal through the epidermis to open on the surface, and, in the meantime, the coiling up of the gradually lengthening gland-tube into a compact ball, and the twisting of the excretory duct as it proceeds to the orifice. The plain muscular tissue of the sweat-glands is said to be developed from some of the epithelium-cells of the rudimentary gland (Ranvier). If this be so, it is the only known instance, in the higher animals, of muscular tissue being developed from the epiblast.

The ceruminous glands in the auditory passage consist of a tube coiled into a ball, like the sweat-glands; and there is such a further correspondence between the two, in structure and mode of development, that the ceruminous glands may be regarded as a variety of the sudoriferous.

It would thus appear that the rudiments of the hair-follicles, sweat-glands, and sebaceous glands, are all derived from the same source. They all originally appear as solid bud-like excrescences of the Malpighian layer of the epidermis, (for the outer stratum of the root-sheath must be regarded as such); these grow into the corium, in which recesses are formed to receive them, and which, of course, yields the material required both for the production of new cells for their further growth, and for the maintenance of their secreting function.

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